

CLONING, 2002

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BEFORE A
SUBCOMMITTEE OF THE
COMMITTEE ON APPROPRIATIONS
UNITED STATES SENATE
ONE HUNDRED SEVENTH CONGRESS
SECOND SESSION

SPECIAL HEARINGS
JANUARY 24, 2002—WASHINGTON, DC
MARCH 12, 2002—WASHINGTON, DC

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CLONING, 2002

THURSDAY, JANUARY 24, 2002

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN
SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 11:01 a.m., in room-192, Dirksen Senate Office Building, Hon. Tom Harkin (chairman) presiding.
Present: Senators Harkin and Specter.

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. This hearing of the Senate Labor, Health and Human Services, and Education Appropriations Subcommittee will come to order. This subcommittee, under the leadership of Senator Specter and I, as we have changed positions over the years, and with the help of our members of the subcommittee, has been committed over these years to helping our top scientists make medical breakthroughs to bring cures for killer diseases like cancer and Alzheimer's, Parkinson's, stroke and other debilitating illnesses and diseases. This hearing is part of that effort, and focuses on the potential of new techniques and how we might bridge deeply held beliefs to find common ground to allow that research to move forward.

As we all know, these are extremely complex issues, and scientists are announcing new advances practically every week. Three years ago, Dr. Michael West of Advanced Cell Technology testified before this committee about a new plan to transplant a patient's DNA into a human egg, grow some stem cells, and then use those cells to cure devastating diseases. It was a plan that immediately brought hope to Americans suffering from Alzheimer's and Parkinson's and juvenile diabetes, and spinal cord injuries, to mention a few.

Well, late last year Dr. Michael West announced that he had taken the first step toward reaching that amazing goal, but with that announcement came a great deal of media attention and, I might add, an avalanche of misinformation about what that advance meant.

Since then, we have learned more about the science behind Dr. West's announcement and the very different potential applications of it. One potential application, of course, is human cloning, a procedure designed to allow the birth of cloned human babies. Human cloning worries most Americans, including us here in Congress, in-

cluding me. I firmly oppose human cloning. I believe it should be banned.

However, the other potential application is far different. Through what I will call therapeutic cellular transfer, or TCT, our scientists may, indeed, unlock the cures for some of our most devastating and debilitating diseases. As I said at our last hearing, I believe it would be tragic to allow our outrage about human cloning to blind us to the promise that TCT holds. Late last week, a distinguished National Academy of Sciences panel made up of many of our Nation's top doctors and researchers, led by Dr. Irving Weissman, who is here today with us, released an important new report that I hope will further assist Senators and Congressmen in understanding the science and crafting a decision about how we should proceed.

This report concludes what we in Congress collectively agree. Human cloning should be outlawed. Stiff penalties should be imposed on anyone who violates this law, but at the same time, this report also makes clear the need for more research to unlock the mysteries of diabetes and Alzheimer's and Parkinson's and these other illnesses. It urges us to allow this potential life-saving research to continue.

So today, Senator Specter and I, joined by other Senators, are introducing legislation that would ban human cloning and impose substantial criminal and civil penalties on any misguided person who would attempt this type of procedure. Our legislation slams the door on human cloning, but keeps it open to life-saving medical research. Our legislation stands in contrast to the position taken by our colleagues in the House, a position which I understand some Senators also advocate. The House bill would also stop vital medical research on stem cells in its tracks. I personally believe that would be a tragic mistake.

It is quite clear that this remains a controversial and contentious issue. There are deeply held beliefs on both sides. We must respect all points of view, and the debate may continue for some time, so let us work together to move forward on what we all agree on. That seems to be the common sense approach we are going to take with the stimulus package. We all agree that human cloning should be banned, so let us do that without further delay.

We are fortunate to have with us this morning an outstanding panel of witnesses that includes scientists on both sides of this issue. Before we hear from them, I would invite my ranking member and my colleague, Senator Specter, to make any opening remarks. Senator Specter.

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Thank you very much, Mr. Chairman. This subcommittee has taken the lead on increasing the funding for the National Institutes of Health from \$12 billion to \$23 billion and has thus enabled the scientific community to make enormous strides against the most dreaded diseases.

When stem cell research was disclosed in November 1998, this subcommittee immediately started a series of hearings, and today's is the 12th in that series. Examining the implication of stem cell research, and what its potential might be. We have worked with our colleagues in the Senate in the face of a Federal prohibition

against using Federal money to extract stem cells from embryos, but permitting Federal funds to be used on stem cell research after the cells were extracted. A distinction which in my judgment does not make a whole lot of sense, and we are moving ahead to try to make Federal funding available for stem cell research generally.

We have 64 Senators who had signed on to broader use of Federal funding on stem cell research, with 12 more Senators being committed to that and willing to put it in writing. Last spring and early summer, President Bush made his noted presentation authorizing the use of Federal funds on stem cells on the 64 existing lines. This subcommittee held further hearings and my view was, I think, shared by our distinguished chairman, that that distinction was too limited, but with the events of 9/11, that has been very much pushed to the sideline.

Then, when there was consideration of the appropriations bill last November, Senator Brownback offered amendments which would not only ban reproductive cloning where there was general agreement that it ought not to be done, but would also ban so-called therapeutic cloning. I believe the scientists made a public relations error of a very severe magnitude in calling it therapeutic cloning. We are now using the term, nuclear transplantation, which is really what it is, as opposed to cloning, which has an opprobrious name and draws immediate adverse reaction.

After a spirited debate on the floor, in consultation with the majority Leader and the minority Leader, Senator Harkin, I, and Senator Brownback agreed to delay the battle until February or March of this year on the issue of nuclear transplantation, and we are moving ahead now to go into that subject in some detail. Senator Harkin has already noted the report of the National Academy of Sciences on scientific and medical aspects of human reproductive cloning, and we shall hear much more about that today from Dr. Irving Weissman.

From the studies that I have undertaken, which have been extensive, it seems to me that it is most unwise for the politicians to limit the scientists on what the scientists can do. Copernicus, Galileo, Pasteur, the scientists which have led us to such remarkable achievements, would have been hamstrung if decisions were to be made in legislative chambers or in town meetings or with the emotional overtone that that imports, but we have worked with all segments, and have invited witnesses today to have a balanced panel in opposition to the views which I have expressed so that we can make a rational judgment.

I noted in this morning's New York Times in an article by Sheryl Gay Stolberg, who has been working on this subject for perhaps as long or longer than the subcommittee has, the conclusions of Ms. Judy Norsigian, a noted author of the book, "Our Bodies, Ourselves," who concludes from a feminist point of view that nuclear transplants place too much of a burden on women. I will be interested to have an amplification on that when the opportunity presents itself, but I think that adds another dimension to the complexity of the issue.

But this is a continuing drama, continuing saga, so stay tuned. We are going to find out all that we can so that when the matter comes up in February or March we are in a position to bring the

best reasoning we can to this very important subject, because millions of lives are at stake. When you talk about nuclear transplantation, you are talking about a procedure where a person who has Parkinson's donates their DNA, which is combined with a donated egg to form an embryo from which derived stem cells will not be rejected when used to cure someone with Parkinson's, Alzheimer's, heart ailments, cancer, or many, many other dreaded diseases.

This is a life or death matter, and we ought not to let ideology determine it. That is my stated determination, and we are moving forward on this important quest.

Thank you, Mr. Chairman.

Senator HARKIN. Thank you, Senator Specter, and for your leadership on this issue.

We will start with our panel. I will introduce them all now, and we will just go down as I read them. First will be Dr. Irving L. Weissman, a professor of cancer biology at Stanford University School of Medicine, the chairman of the National Academy of Sciences panel that just released the report on the scientific and medical aspects of human cloning. Dr. Weissman received his M.D. from Stanford University.

We welcome you, Dr. Weissman. Your statement will be made a part of the record in its entirety, and we ask if you might please sum it up for us. I would appreciate that. Dr. Weissman.

STATEMENT OF IRVING WEISSMAN, M.D., PROFESSOR, STANFORD UNIVERSITY

Dr. WEISSMAN. Thank you.

Mr. Chairman and members of the subcommittee, my name is Irv Weissman. I am a professor at Stanford Medical School, and my main research field for the last 20 years has been the biology and transplantation of adult stem cells in mice and humans. I am here as chair of the National Academy's panel on scientific and medical aspects of human cloning, which released its report on January 18, 2002.

The charge to the panel in June 2001 was to examine the scientific and medical issues relative to human and reproductive cloning, including the protection of human subjects, and to clarify how human reproductive cloning differs from stem cell research. Our charge did not extend to an examination of the ethical issues related to human reproductive cloning.

We needed to determine whether current methods for reproductive cloning are scientifically feasible and reproducible and medically safe. In addition, we needed to examine whether human participants in the process could be adequately advised and protected. Society and its leaders will need such scientific and medical information if they are to address the relevant ethical and public policy issues.

In reproductive cloning, the nucleus of a body cell is transplanted into an egg whose nucleus has been removed, stimulating it to divide to produce a roughly 150-cell blastocyst embryo. The blastocyst is then placed into a uterus with the intent of creating a newborn.

In a related but different procedure, cells are isolated from a blastocyst derived by nuclear transplantation, and the cells are

used to produce stem cell lines. Such stem cells are unspecialized cells that can develop into almost all kinds of body cells.

In what is sometimes called therapeutic cloning, the donor of a nucleus for transplantation to produce stem cells can be a person in whom the stem cell daughter cells will be used to regenerate damaged tissues.

But there is another medical use for transplantation to produce stem cells. Stem cells derived from a body cell or a diseased cell of a patient who had inherited the risk for that disease could be powerful tools for medical research and lead to improved therapies.

We studied the scientific and medical literature, and held a workshop with world leaders in the relevant technologies. Among the participants were persons who planned to clone human beings. The data from animal studies of reproductive cloning demonstrate that only a small percentage of the attempts are successful, that many of the resulting clones die during all stages of gestation pregnancy, that newborn clones often are abnormal, or die, and that the procedures carry serious risks for the mother. However, the data on nuclear transplantation to produce stem cells show that these cells are functional.

Given these findings, the panel unanimously approved the following recommendations. Human reproductive cloning should not now be practiced. It is dangerous, and likely to fail. The panel therefore unanimously supports the proposal that there should be a legally enforceable ban on the practice of human reproductive cloning.

The scientific and medical considerations—that is what we considered—related to the ban should be reviewed within 5 years. The ban itself should be reconsidered only if these two conditions are met. First, a new scientific and medical review indicates that the procedures are likely to be safe and effective and, second, a broad national dialogue on the societal, religious, and ethical issues suggests that a reconsideration of the ban is warranted.

Finally, the scientific and medical considerations that justify a ban on human reproductive cloning at this time are not applicable to nuclear transplantation to produce stem cells. Because of the considerable potential for developing new medical therapies for life-threatening diseases, and advancing fundamental knowledge, the panel supports the conclusion of a recent National Academy report that recommended that biomedical research using nuclear transplantation to produce stem cells be permitted. A broad national dialogue on the societal, religious, and ethical issues is encouraged in this matter.

So that is the end of our recommendations.

Scientists place high value on the freedom of inquiry, a freedom that underlies all forms of scientific and medical research. Recommending restrictions of research is a serious matter, and the reasons for such a restriction must be compelling. In the case of human reproductive cloning, we are convinced that the potential dangers to the implanted fetus, to the newborn, and to the woman carrying the fetus constitute just such compelling reasons. In contrast, there are no scientific or medical reasons to ban nuclear transplantation to produce stem cells, and such a ban would certainly close avenues of promising scientific and medical research.

The panel stressed that all concerned segments of society should examine and debate the broad societal and ethical issues associated with human reproductive cloning as well as those associated with nuclear transplantation to produce stem cells. We hope our report will help this subcommittee and President Bush's Council on Bioethics in this regard.

PREPARED STATEMENT

Thank you for the opportunity to testify. I am glad that this statement, and I hope the panel report also, can be placed into the record. I will be happy to answer any questions.
[The statement follows:]

PREPARED STATEMENT OF IRVING L. WEISSMAN

Mr. Chairman and members of the Subcommittee. My name is Irv Weissman. I am a professor at Stanford Medical School, and my main research field for the last 20 years has been the biology and transplantation of adult stem cells in mice and humans. I am here as chair of the National Academies Panel on Scientific and Medical Aspects of Human Cloning, which released its report on January 18, 2002.

The charge to the panel in June 2001 was to examine the scientific and medical issues relevant to human reproductive cloning, including the protection of human subjects, and to clarify how human reproductive cloning differs from stem cell research. Our charge did not extend to an examination of the ethical issues related to human reproductive cloning.

We needed to determine whether current methods for reproductive cloning are scientifically feasible and reproducible and are medically safe. In addition, we needed to examine whether human participants in the process could be adequately advised and protected. Society and its leaders will need such scientific and medical information if they are to address the relevant ethical and public-policy issues.

In reproductive cloning, the nucleus of a body cell is transplanted into an egg whose nucleus had been removed, stimulating it to divide to produce a blastocyst embryo; the blastocyst is then placed into a uterus with the intent of creating a newborn.

In a related but different procedure, cells are isolated from a blastocyst derived by nuclear transplantation, and the cells are used to produce stem cell lines. This is shown in the figure. Such stem cells are unspecialized cells that can develop into almost all kinds of body cells. In what is sometimes called therapeutic cloning, the donor of a nucleus for transplantation to produce stem cells can be a person in whom stem cell daughter cells will be used to regenerate damaged tissues. There is another medical use for nuclear transplantation to produce stem cells; stem cells derived from a body cell or a disease cell of a patient who had inherited the risk for that disease could be powerful tools for medical research and lead to improved therapies.

We studied the scientific and medical literature and held a workshop with world leaders in the relevant technologies. Among the participants were persons who planned to clone human beings. The data from animal studies of reproductive cloning demonstrate that only a small percentage of the attempts are successful, that many of the resulting clones die during all stages of gestation, that newborn clones often are abnormal or die, and that the procedures carry serious risks for the mother. However, the data on nuclear transplantation to produce stem cells show that these cells are functional.

Given those findings, the panel unanimously approved the following recommendations:

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Finally, the scientific and medical considerations that justify a ban on human reproductive cloning at this time are not applicable to nuclear transplantation to produce stem cells. Because of the considerable potential for developing new medical

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The panel stressed that all concerned segments of society should examine and debate the broad societal and ethical issues associated with human reproductive cloning, as well as those associated with nuclear transplantation to produce stem cells. We hope our report will help this Subcommittee and President Bush's Council on Bioethics in this regard.

Thank you for the opportunity to testify. I hope that my statement and the panel report can be put into the record. I will be happy to answer questions.

Senator HARKIN. Dr. Weissman, thank you very much.

Next, we call on Dr. Rudolf Jaenisch, a founding member of the Whitehead Institute, and a professor of biology at the Massachusetts Institute of Technology. Dr. Jaenisch received his M.D. from the University of Munich. He has done extensive research with mice on cancer and on cloning.

Dr. Jaenisch, welcome. Please proceed.

STATEMENT OF RUDOLF JAENISCH, M.D., PROFESSOR, MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Dr. JAENISCH. Thank you, Mr. Chairman. I am a professor of biology at the Whitehead Institute, and I am a basic scientist with a long-term interest in embryonic development and recently in the cloning of mice. I do not work with human embryonic stem cells or therapeutic cloning, but these are the two issues I want to comment on.

First, reproductive cloning. Last year, I gave testimony before the House and the Senate subcommittee, and for scientific reasons I warned human cloning would be irresponsible and reckless. Together with Ian Wilmut, I wrote an article for *Science* where we summarized our concerns, and I would like to submit this article for the record.

Senator HARKIN. Without objection.
[The information follows:]

[From *Science*, March 2001]

DON'T CLONE HUMANS!

(By Rudolf Jaenisch and Ian Wilmut)*

The successes in animal cloning suggest to some that the technology has matured sufficiently to justify its application to human cloning. An in vitro fertilization specialist and a reproductive physiologist recently announced their intent to clone babies within a year's time.¹ There are many social and ethical reasons why we would never be in favor of copying a person. However, our immediate concern is that this proposal fails to take into account problems encountered in animal cloning.

*R. Jaenisch is at the Whitehead Institute for Biomedical Research and Department of Biology, MIT, Cambridge, MA 02142, USA. I. Wilmut is at the Roslin Institute, Roslin, Midlothian EH25 9PS, UK.

¹A. Stern, *Boston Globe*, 27 January 2001, p. A7.

Since the birth of Dolly the sheep,² successful cloning has been reported in mice,³ cattle,⁴ goats,⁵ and pigs,^{6,7} and enough experience has accumulated to realize the risks. Animal cloning is inefficient and is likely to remain so for the foreseeable future. Cloning results in gestational or neonatal developmental failures. At best, a few percent of the nuclear transfer embryos survive to birth and, of those, many die within the perinatal period. There is no reason to believe that the outcomes of attempted human cloning will be any different. The few cloned ruminants that have survived to term and appear normal are often oversized, a condition referred to as "large offspring syndrome".⁸ Far more common are more drastic defects that occur during development. Placental malfunction is thought to be a cause of the frequently observed embryonic death during gestation. Newborn clones often display respiratory distress and circulatory problems, the most common causes of neonatal death. Even apparently healthy survivors may suffer from immune dysfunction, or kidney or brain malformation, which can contribute to death later. So, if human cloning is attempted, those embryos that do not die early may live to become abnormal children and adults; both are troubling outcomes.

The fetal abnormalities and abnormalities in those few clones that are born live are not readily traceable to the source of the donor nuclei. The most likely explanation may be failures in genomic reprogramming. Normal development depends upon a precise sequence of changes in the configuration of the chromatin and in the methylation state of the genomic DNA. These epigenetic alterations control tissue-specific expression of genes. For cloning technology, the crucial question is a simple one: Is the configuration of chromatin changes acquired by a donor nucleus in the injected oocyte functionally identical to that resulting from gametogenesis and fertilization?

Epigenetic reprogramming is normally accomplished during spermatogenesis and oogenesis, processes that in humans take months and years, respectively. During nuclear cloning, the reprogramming of the somatic donor nucleus must occur within minutes or, at most, hours between the time that nuclear transfer is completed and the onset of cleavage of the activated egg begins. Prenatal mortality of nuclear clones could be due to inappropriate reprogramming, which could lead in turn to dysregulation of gene expression. Some long-term postnatal survivors are likely to have subtle epigenetic defects that are below the threshold that threatens viability.

Circumstantial evidence begins to hint at defects in programming of gene expression in cloned animals.^{9,10} Expression of imprinted genes was significantly altered when mouse or sheep embryos were cultured in vitro before being implanted into the uterus.^{11,12} Thus, even minimal disturbance of the embryo's environment can lead to epigenetic dysregulation of key developmental genes. Also, preliminary observations suggest that widespread gene dysregulation in cloned mice is associated with neonatal lethality.¹³

There is every reason to think that the human cloning experiments announced by P. Zavos and S. Antinori will have the same high failure rates as laboratories have experienced when attempting animal cloning. Zavos tried to reassure the public by saying that: "We can grade embryos. We can do genetic screening. We can do quality control."¹ The implication is that they plan to use the methods of routine prenatal diagnosis employed for the detection of chromosomal and other genetic abnormalities. However, there are no methods available now or in the foreseeable future to examine the overall epigenetic state of the genome.

Public reaction to human cloning failures could hinder research in embryonic stem cells for the repair of organs and tissues. Research is being conducted into programming these cells to turn into specific tissues types, which could (for example) be used to regenerate nerve cells and those in the heart muscle, benefiting patients with Parkinson's, Alzheimer's, and heart disease. The potential benefit of this therapeutic cell cloning will be enormous, and this research should not be associated with the human cloning activists.

²I. Wilmut et al., *Nature* 385, 810 (1997).

³T. Wakayama et al., *Nature* 394, 369 (1998).

⁴Y. Kato et al., *Science* 282, 2095 (1998).

⁵A. Baguisi et al., *Nature Biotech.* vol. 17, 456 (1999).

⁶I. Polejaeva et al., *Nature* 407, 86 (2000).

⁷A. Onishi et al., *Science* 289, 1188 (2000).

⁸L. E. Young et al., *Rev. Reprod.* 3, 155 (1998).

⁹P. De Sousa et al., *Cloning* 1, 63 (1999).

¹⁰R. Daniels et al., *Biol. Reprod.* 63, 1034 (2000).

¹¹S. Khosla et al., *Biol. Reprod.* 64, 918 (2001).

¹²L. E. Young et al., *Nature Genet.* 27, 153 (2001).

¹³R. Jaenisch et al., unpublished observations.

We believe attempts to clone human beings at a time when the scientific issues of nuclear cloning have not been clarified are dangerous and irresponsible. In the United States, the National Bioethics Advisory Commission¹⁴ reached that conclusion 5 years ago, "At present, the use of this technique to create a child would be a premature experiment that would expose the fetus and the developing child to unacceptable risks." All the data collected subsequently reinforce this point of view.¹⁵

Dr. JAENISCH. Over the last year, we and others have gathered hard molecular data, and today we can state with certainty that there are widespread abnormalities in gene expression in cloned animals. The new data are entirely consistent with my belief that even without overt disease, most or all cloned animals will have defects of one kind or another, so in summary, all evidence from animal experiments argues that reproductive cloning of humans is irresponsible and should not be pursued.

I support, however, therapeutic applications of nuclear transfer, sometimes called therapeutic cloning, or TCT. The therapeutic cloning approach combines nuclear transfer and embryonic stem cells. Embryonic stem cells derived from early embryos, and they are capable of generating any cell type of the body, and can provide unlimited tissue types that can be used for tissue replacements in conditions such as Parkinson's, or liver cirrhosis, or Alzheimer's.

Therapeutic cloning combines these two techniques with nuclear transfer with the goal of creating a customized stem cell line for a needy patient. For instance, if one of you is severely diabetic, this approach would take a cell, let us say from a skin biopsy, take the nucleus from this skin cell, and transfer this nucleus into an egg from which its own nucleus had been removed. If the nucleus of your skin cell is exposed to the nucleus from the egg, it reverts to its embryonic state. Your skin cell begins to re-express those genes that it expressed when it, itself, was an embryo. Whether this cell that results from this process is a new embryo or a skin cell rejuvenated is as much a question of philosophy as of science.

The cloned cells are cloned in a Petri dish. They give rise to an embryonic stem cell line that can be induced to insulin-producing cells and then planted into you, not rejected, because they are from your own body.

Therapeutic cloning raises scientific and ethical concerns, and I want to address some of these concerns that have been subject to public debate that often ignores underlying scientific and biological issues.

First, an important concern is that the use of embryos that have the potential to develop into a human being is the source to derive a cell line. I want, based upon biological facts, to emphasize a critical distinction between therapeutic cloning and the derivation of embryonic stem cells from a fertilized embryo which was generated by in vitro fertilization. I should remind you that all existing human embryonic stem cells have been derived from IVF embryos. In IVF, the embryo has a unique combination of genes that has not existed before and will not exist again, and secondly, this embryo has a very high potential to develop into a healthy baby if implanted.

¹⁴NBAC, Executive Summary, Cloning Human Beings <http://bioethics.gov/pubs.html>, p. ii (June 1997).

¹⁵We thank R. Weinberg, G. Fink, D. Page, A. Chess, W. Rideout, L. Young, H. Griffin, and L. Paterson.

In therapeutic cloning, the embryo first has the identical combination of genes as the donor. Therefore, the cloned embryo does not represent the creation of a new, unique life form, but, rather, the programming and rejuvenation of an existing cell from your body. One could argue it is a special form of transplantation.

Second, the cloned embryo has a very low potential to ever develop into a normal person, if implanted, because the overwhelming majority of clones do not gestate normally, and will be abnormal.

The generation of embryonic stem cells from cloned blastocysts for the purpose of therapeutic cloning would appear to me to pose fewer ethical problems than the generation of embryonic stem cells from an in vitro fertilized embryo. The majority of people in this country appear to accept the generation of embryonic stem cells from left-over IVF embryos if they are not implanted and would be destined for destruction.

Another concern is that most animals derived by nuclear transfer have serious abnormalities and die early in development, and probably some of these abnormalities are related to abnormal imprinting. This begs the question, would differentiated cells derived from a cloned embryonic stem cell cause similar abnormalities when transplanted to a patient?

Now, from all the evidence we have gathered over the last year from our own laboratory and from others, I think I can state with confidence that there are no principal scientific reasons that would limit the use of embryonic stem cells for tissue repair.

An alternative to embryonic stem cells has attained much attention, which are adult stem cells. Can they provide another source for transplantation? Adult stem cells are derived from a variety of tissues. They have a surprising property to differentiate into functional nerve cells or heart cells that could be transplanted. The question is whether the promise of adult stem cells is so great as to eliminate a need for research on embryonic stem cells.

The field of adult stem cells is very exciting, but very young indeed. With the exception of bone marrow cells, stem cells, most adult somatic stem cells from other tissues remain poorly defined, difficult to purify, and cannot be grown in culture, and their clinical value has not been established. In contrast, embryonic stem cells have been intensely studied for more than 20 years, can be grown indefinitely in culture in some homogenous populations, and have been shown to generate all tissue types of the body.

To conclude, it would be unfortunate to stop research on embryonic stem cells because of the unrealized potential of adult stem cells. Research in both fields should proceed with high priority.

How do other countries deal with this problem? I think the British solution is a very reasonable one. Cloning of a human embryo for the purpose of creating a person, reproductive cloning, is criminal, but cloning of an embryo for therapeutic purposes is permitted. The dividing line between criminal and permitted manipulation is a clear one, implantation of the cloned embryo into the womb. Implantation of a cloned embryo is not permitted, is criminal, but its plantation into a Petri dish is permitted. I believe that this dividing line between criminal and permitted manipulation is clearly defined, and makes biological sense.

The main question U.S. legislators have to struggle with when making a decision is this one. Do we want to close a door to the most advanced and promising research and deny many known suffering patients the route for potential cure?

To criminalize therapeutic cloning in this country poses serious ethical problems. Given that adult stem cell research is in its infancy and cannot be predicted what or when therapeutic application will be delivered, can we afford to wait until this field has matured? Do you want to tell patients who now suffer debilitating diseases that they will have to wait for an unspecified number of years until the technical problems of adult stem cells may have been resolved? In contrast, a patient with the same disease in Britain may be able to use a stem-cell-based therapy in a few years to come.

Unfortunately, the public discussion of therapeutic cloning suffers from serious misconceptions. Often, reproductive cloning is not differentiated from therapeutic cloning. The word, cloning, provokes negative emotional reactions. A better term would be, indeed, nuclear transplantation of stem cells.

I am concerned that the revulsion against reproductive cloning rather than objective reasons may lead to legislative actions that might impede potentially promising research. It would be unfortunate, indeed, if legislative decisions would be based on emotion rather than objective criteria.

I want to make a final point. In the 1970s, when IVF became available as a reproductive technology, federally funded research was not permitted in this country, in contrast to European countries. The result was that IVF was practiced in the private sector and lacked proper supervision. As a consequence, even today, the activities of many fertility clinics are obscure, unsupervised, and lack public scrutiny.

PREPARED STATEMENT

It would be unfortunate if a similar mistake were made with therapeutic cloning. I believe you should proceed with this research under tight regulation. The work should be supported by Federal funding, and peer reviews should be conducted in academic institutions of the highest standing that are bound to follow scientific and ethical standards and are subject to public scrutiny.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF RUDOLF JAENISCH

I am a professor of biology at the Whitehead Institute and MIT, Boston. I am a basic scientist with a long-term interest in understanding the mechanisms of mammalian development. In recent years my research has focused on the cloning of mice with the goal to understand the reasons why the great majority of cloned animals are abnormal. Most of my funding comes from Federal sources through peer reviewed grants from the NIH. My laboratory does not use human ES cells nor is it involved with the reproductive or therapeutic cloning of humans. These are, however, the two issues I want to address in my remarks.

REPRODUCTIVE CLONING

In March last year I gave testimony before the House Subcommittee on Energy and Commerce and before the Senate Subcommittee on Commerce, Science and Space: for scientific reasons I warned that any proposal to create humans by cloning

would be irresponsible and reckless. Together with Ian Wilmut, who generated Dolly, I wrote an article for Science magazine where we summarized our concerns and I would like to submit that article for the records. Last year, no concrete evidence on gene expression in cloned animals was available and we could not base our opinion on hard molecular data. Since last year we and others have gathered hard molecular data and today we can state with certainty that there are widespread abnormalities in gene expression in cloned animals. For example, a recent study published in Science found that the expression patterns of a majority of the genes examined in the placentas of cloned mice were abnormal. These new data are entirely consistent with my belief that even without overt disease, virtually all cloned animals will have defects of one kind or another. Activists who push for human cloning at this point in time ignore the very worrisome scientific evidence that cloning is unsafe.

In summary, all evidence from animal experiments argues that reproductive cloning of humans is irresponsible and should not be pursued

My stance is clear: As a matter of science and as a personal conviction, I am opposed to human reproductive cloning. However, I am just as staunchly supportive of therapeutic applications of nuclear transfer, sometimes called therapeutic cloning. I believe it would be unfortunate if the door was closed to therapeutic cloning, as this would have grave consequences for an extremely promising new field of medical research. This is the topic I want to focus on.

THERAPEUTIC CLONING

The therapeutic cloning approach is based on embryonic stem cells as discussed below.

Embryonic Stem cells.—These cells are derived from early embryos and they are cells capable of generating any cell type of the body. Discovered 20 years ago in mice and subject to extensive research, we can predict today with some confidence that these cells can provide unlimited number of cells of any tissue type that can be used for tissue replacement in conditions such as Parkinsons, diabetes, Alzheimers, liver cirrhosis etc. The available evidence suggests that human embryonic stem cells have a similar potential.

Therapeutic cloning.—The technique of therapeutic cloning combines nuclear cloning and embryonic stem cell research, with the goal of creating a customized stem cell line for a needy patient. For instance, if one of you is severely diabetic, in this approach we would begin by taking one of your cells, perhaps from a skin biopsy or blood sample, and isolate its nucleus the core of the cell that carries the chromosomes and all the genetic material. We would then inject your nucleus into an egg whose own nucleus, or genetic material, has been removed. The egg might come from a family member, a wife or daughter who would view the egg donation in the same light as a donation of an organ, a kidney or a liver or perhaps bone marrow or blood. When the nucleus of your skin or blood cell is exposed to signals in the egg, it reverts to its embryonic state and your skin or blood cell begins to re-express the genes that it expressed when it was an embryo. Whether the cell that results from this process is your skin cell rejuvenated or a new embryo is as much a question of philosophy as of science. The methods are similar to the initial manipulations in reproductive cloning, but the intent is to generate cells for transplantation, not a human being. The cloned cells are grown in the petri dish for a few days, and instead of being implanted into the uterus of a woman, are cultured to generate an embryonic stem cell. This ES cell would match your body perfectly because it is your tissue. We would then coax the ES cells to differentiate in culture to insulin-producing cells, that we could then implant into you without fearing rejection and without the need to treat you with immune suppressive agents. Thus, the embryonic stem cells created by therapeutic cloning are of exclusive benefit to you—the nuclear donor and the recipient of the therapy patient. This contrasts with conventional organ transplantations where often poorly matched donors have to be used leading to major complications due to organ rejection and the use of immunosuppressive drugs.

Therapeutic cloning raises scientific and ethical concerns and I want to address some of these concerns that have been subject to a public debate that often ignores the underlying scientific and biological issues. The following questions are relevant for the potential use of the technology for tissue replacement in human patients.

1. An important issue in this debate is the concern of using embryos that have the potential to develop into a human being as a source for the generation of a cell line. I want, based upon biological facts, to emphasize a critical distinction between therapeutic cloning and the derivation of embryonic stem cells from a fertilized embryo derived by in vitro fertilization (IVF). All existing human embryonic stem cells

have been derived from IVF embryos that were not implanted into the uterus. I want to stress two important differences between embryonic stem cells created by IVF or by therapeutic cloning.

(a.) *In IVF* the embryo (i) has a unique combination of genes that has not existed before and (ii) has a high potential to develop into a healthy baby when implanted.

(b.) *In therapeutic cloning* the embryo (i) has the identical combination of genes as the donor. Therefore, the cloned embryo does NOT represent the creation of a unique new life but rather the reprogramming and rejuvenation of an existing cell from your body. One could argue that this is a special form of autologous transplantation meaning derived from one's own tissues, which is already widely used in bone marrow, blood, and skin transplantation. (ii) The cloned embryo has a very low potential to ever develop into a normal person, because the overwhelming majority of clones do not gestate normally.

The majority of people in this country appear to accept the generation of embryonic stem cells from "left over" IVF embryos that are not implanted into the womb but would be destined for destruction. The generation of embryonic stem cells from cloned blastocysts for the purpose of therapeutic cloning would appear to pose fewer ethical problems than the generation of embryonic stem cells from IVF embryos.

2. Most animals cloned by nuclear transfer have serious abnormalities and die early in development. This begs the question: Would differentiated cells derived from embryonic stem cells that have been created by nuclear transfer cause similar abnormalities when transplanted into a human patient? Another question was raised by results from my laboratory showing that an important class of embryonically regulated, imprinted genes are dysregulated in mouse embryonic stem cells, a condition termed epigenetic instability. This evoked an additional concern: Does the epigenetic instability of imprinted genes interfere with their potential use in tissue replacement?

The most serious abnormalities in cloned animals are caused by faulty reprogramming leading to abnormal regulation of genes that are important for the development of a whole embryo. In contrast, when an embryonic stem cell is differentiated in culture to functional tissue cells such as nerve cells, heart muscle cells or beta cells of the pancreas, these developmental genes need not be expressed (because no embryo is generated). Similarly, the faithful expression of imprinted genes is crucial for embryonic development but has probably little if any role for the proper functioning of adult somatic cells. Therefore, problems seen in cloned animals are not expected to affect the function of cells that are derived from cloned embryonic stem cells.

I want to emphasize the difference between generating a cloned animal from a embryonic stem cell nucleus by cloning and the transplantation of differentiated cells derived from the embryonic stem cells. In cloning, the donor nucleus must direct the development of an embryo and of all organs, and faulty reprogramming of the genome causes serious abnormalities in the cloned animal. This is not the case in tissue transplantation where the cells derived from the embryonic stem cell are introduced into a patient, i.e. in an organism that has been derived from a fertilized egg. The extensive experience with mouse embryonic stem cells over the last 20 years indicates that no abnormalities arise when ES cells are introduced into a normal embryo to form "chimeric mice" (as routinely used for gene targeting) or into an adult mouse. Therefore, it is not to be expected that epigenetic instability, if indeed found to be a property of human ES cells, would create a problem for transplantation.

In summary, I do not see principal scientific reasons that would limit the use of ES cells for tissue repair

Adult stem cells.—An alternative to embryonic stem cells that has attracted much attention are adult stem cells: can they provide another source for transplantation? Adult stem cells are isolated from a variety of tissues. They have the surprising ability to differentiate into functional cells such as nerve cells or heart muscle cells and even may have the potential to generate functional cells of tissue types other than that of their own origin. The hope is that such cells can be isolated from the adult and can serve as a source for transplantation. As with therapeutic cloning, the cells would be accepted by the patient but their generation would not involve the creation of a cloned embryo and thus would pose no ethical problems.

Clearly, the recent work on adult stem cells is very exciting and may even be revealing novel biological paradigms. Research on adult stem cells should be supported with great vigor. The question however, is whether the promise of adult stem cells to provide tissue repair is so great as to eliminate the need for research on embryonic stem cells. As a scientist with a broad perspective on these issues, let me give you my opinion.

The field of adult stem cell research is really very young. With the exception of bone marrow stem cells, which have been used for decades in bone marrow transplantation in the clinic, most adult somatic stem cells of other tissues were discovered only in the past few years and they remain poorly defined. Adult somatic stem cells for the brain, liver, pancreas, and skin among others are rare, difficult to purify and in most cases, are challenging to grow in culture. Adult stem cells have not been found in all tissues, and the clinical value of the ones we have at hand has not been established.

Embryonic stem cells have been intensively studied for more than 20 years. Embryonic stem cells, in contrast to adult stem cells, grow indefinitely in culture as homogeneous populations and have been shown to generate all tissue types of the body. Much progress has been made to direct differentiation to desired tissue types. Thus, we can be confident that embryonic stem cells represent the precursors of all tissues and that through research, tissue replacement will be realized in the future.

In conclusion, it would be unfortunate to stop research on embryonic stem cells because of the unrealized potential of adult stem cells. Research in both fields should proceed with high priority

The British solution to embryonic stem cell work and therapeutic cloning is a reasonable one: Cloning of a human embryo for the purpose of creating a person (reproductive cloning) is criminal but cloning of an embryo for therapeutic purpose is permitted (therapeutic cloning). The dividing line between criminal and permitted cloning is a clear one: the implantation of the cloned embryo into the womb. Implantation of a cloned embryo is not permitted but explantation into a petri dish with the intent to derive an embryonic stem cell for therapeutic purpose is permitted. I believe that this dividing line between criminal and permitted manipulation of a human embryo is clearly defined and makes biological sense.

The main question you as legislators have to struggle with when making a decision is this one: do you want to close the door to the most advanced and promising research and deny the many now suffering patients a route for potential cure? To criminalize therapeutic cloning in this country poses serious ethical problems. Given that adult stem cell research is still in its infancy and it cannot be predicted what or when a therapeutic application will be delivered, can we afford to wait until this field has matured? Do you want to tell patients who suffer NOW of incurable and debilitating diseases that they will have to wait for an unspecified number of years until the technical problems of adult stem cells may have been resolved? In contrast, a patient with the same disease in Britain may be able to use a stem cell based therapy in a few years to come.

Unfortunately, the public discussion of therapeutic cloning suffers from serious misconceptions. Often, "reproductive cloning" is not differentiated from "therapeutic cloning". The word "cloning" provokes negative emotional reactions. I am concerned that the revulsion against "cloning" rather than objective reasons may lead to legislative actions that might impede potentially promising research. A case in point is "nuclear magnetic resonance imaging" or "NMRI". This technique, now known as "MRI", became widely used in the clinic as diagnostic procedure only after the word "nuclear" was dropped from its designation (because no radioactive substance is used). It would be unfortunate indeed if legislative decisions would be based on emotional rather than objective criteria.

I want to make a final point. In the 70s, when IVF became available as a reproductive technology, federally funded research was not permitted in this country in contrast to European countries. The result was that IVF was practiced in the private sector and lacked proper supervision. As a consequence, even today the activities of many fertility clinics are unsupervised and lack public scrutiny. It would be unfortunate if a similar mistake were made with therapeutic cloning. I believe we should proceed with this research under tight regulation. The work should be supported by Federal funding, peer reviewed and be conducted in academic institutions of the highest standing that are bound to follow scientific and ethical standards and are subject to public scrutiny.

Senator HARKIN. Dr. Jaenisch, thank you very much for your statement.

Dr. Blackwelder is president of Friends of the Earth, a national organization dedicated to preserving the environmental health and diversity of the planet. Dr. Blackwelder received his B.A. from Duke University, M.A. from Yale, and Ph.D. from the University of Maryland. He is an advocate for expanding the national wild and scenic systems. Dr. Blackwelder, welcome, and please proceed.

STATEMENT OF DR. BRENT BLACKWELDER, PRESIDENT, FRIENDS OF THE EARTH

Dr. BLACKWELDER. Thank you very much, Mr. Chairman. I might mention that I have spent the past 30 years as an environmental advocate working for a number of environmental organizations. My doctorate from the University of Maryland is in the area of philosophy. My specialty is ethics. I wrote my dissertation on duties to animals, so I feel especially geared to give this testimony for you today, because I want to lay out for you the environmental case for banning reproductive cloning and putting a moratorium on therapeutic cloning.

Basically, the case is that these actions violate two fundamental cornerstone principles of the modern environmental movement: respect for nature and the precautionary principle. But at the outset, I want to point out that the debate is being framed as one being between those who want to make tremendous progress in alleviating human suffering, curing some of the most terrible diseases humanity now faces, and those who want to block medical progress, and I think that is the wrong way to look at the momentous decisions that we are about to make, because we are, in fact, dealing with decisions that will take us in the direction, potentially, of commodifying all life on earth.

We have already seen things going on now with genetic engineering in agriculture, and now proposals with humans that cross the species barriers and take us in the direction of a totally manufactured world. What we want to also emphasize is that not only are we dealing with two types of cloning, reproductive and therapeutic cloning, but we are also dealing with those who want to work on inheritable genetic modifications, the so-called designer babies, a subject which has, in fact, been discussed in *Sports Illustrated* as bringing the end to athletics, if you can engineer super human beings.

I think this is a big cluster of issues, and therefore we are urging, with the precautionary principle, that you actually take a deep and hard look at some of the things going on.

So with that, let me just describe these two principles to you. Environmental organizations embrace the idea of respect for nature because we carry on many activities. Groups run nature centers, conduct lots of education programs and so forth, take people on nature outings. We strive to demonstrate the interdependence of humans in the natural world, and the value of each species' contribution to the entire ecosystem. If a species is altered or wiped out, that can affect the entire ecosystem.

We think the very act of cloning animals or people crosses the threshold of respect for the individuality of the species, and the features of the individuals within each species. That principle leads us to oppose the full-scale commodification of nature, whether it be humans, animals, plants, or landscapes.

Now, even though many in the biotechnology businesses assert that their only goal is curing disease and saving human lives, I want to assure you that there are many others out there, published in the literature, and whom we have debated on national television, that have a much broader agenda. They have the designer baby syndrome and the cloning of human beings fully on their intent.

They have said so on national TV. You may think you are banning one form of cloning and allowing the other to go forward, but we very much want to point out that the Feinstein-Kennedy bill, for example, does not provide roadblocks in the way of crossing those barriers, and we attach to our testimony a critique done by the International Center for Technology Assessment, and I put in my testimony some of the quotes from people who have written books like *Remaking Eden*, that this is not theoretical concern that we have, it is a real, genuine one, and it leads directly into the second point I want to make, which is the precautionary principle.

The precautionary principle basically takes the wisdom of the ages, the old adages, look before you leap, an ounce of prevention is worth a pound of cure. We do not want to go forward with actions that impose risks on others or on society as a whole. We have got to know what we are doing. This is not an antiscientific point of view. We are very progressive, we think, at Friends of the Earth as an organization, but we take a review of the past 100 years of fiascoes, with introduced species, civil works projects, agricultural experiments, medicine and disease, and we ask you in this testimony, don't these exemplify worst-case scenarios materializing, whereas individuals today are saying, well, we have got a best-case scenario, we are going to really cure all these diseases.

We are saying, if you take a look at some of these examples you will find a different story, and I might just point out that the Office of Technology Assessment has indicated that the cost of these invasive alien or exotic species which have been, in some cases, deliberately introduced over the past 100 years, costs the economy now \$100 billion.

Just take a look. The Department of Agriculture introduced the chestnut blight into the United States because they had a subdivision that wanted to put new species in. They brought the Asian chestnut in. Very quickly, the most valuable tree in the Eastern United States for wildlife, and commercially, was wiped out, and to this day there is no cure for that chestnut blight. I mean, that was done with the best of all intentions, but look at the horror and tragedy to the forests.

I point out, for example, that in the Great Lakes since 1829, there have been over 100 alien or invasive exotic species put in. Two of those, like the beaver mussel and the lamprey are with us today, causing tens of millions of dollars worth of damage.

If you turn, for example, to genetically engineered crops, Friends of the Earth was the one that had to point out that the Starlink corn, the genetically engineered starlink corn, not approved for human consumption, only for animals, got into our food supply. Well, that surely shows the failure of a regulatory regime, so you may hope that some of these therapeutic clones do not go the other direction, but the track record is not great.

Just another example, mad cow disease, vigorously denied by British authorities as to have any jumping capability to humans, and yet it did jump, and now they are sorry. Now we have got a serious problem spread to Europe.

PREPARED STATEMENT

These ought to introduce into our thinking the idea that the best-case scenario is not always the one we ought to explore, and so in my testimony I try to lay that out for you, and I just want to conclude—I see my time is up—by quoting from the great environmental naturalist Aldo Leopold, who wrote “The Sand County Almanac,” and he said, “the human role of conqueror, where we are in this role, eventually is self-defeating, because it is implicit in such a role that the conqueror knows, ex cathedra, just what makes the community clock tick, just what and who is valuable, and what and who is worthless in community life. It always turns out that he knows neither, and this is why his conquests eventually defeat themselves.”

I am prepared to answer questions for you. Thank you very much for the opportunity to testify.

[The statement follows:]

PREPARED STATEMENT OF DR. BRENT BLACKWELDER

INTRODUCTION

Friends of the Earth is a national conservation organization dedicated to a cleaner, healthier planet for all life on earth. We are part of Friends of the Earth International which has member groups in 69 countries. I have been President of Friends of the Earth since 1994. My doctorate is in philosophy from the University of Maryland, with ethics being my field of specialization.

The Senate is now considering long-overdue legislation to ban human cloning. The debate is being framed as one between modern medical science seeking new technologies for the prevention and treatment of disease and those who are trying to block medical progress. The purpose of the Friends of the Earth testimony is to present the environmental case against both human cloning and the closely related issue of human germline manipulation or inheritable genetic modifications (“designer babies”).

At the outset I wish to note that Friends of the Earth acknowledges that many applications of human genetic science, including those using stem cells, hold great medical promise. However, the rapid pace of development of new technologies, the enormous stakes involved, the lack of societal controls to date, the failure to analyze environmental implications, and the fact that informed public debate has barely begun, all indicate the need for immediate legislative action to ban the creation of full-term human clones (reproductive cloning) and at least to place a moratorium on the creation of clonal human embryos for research purposes (therapeutic cloning).

Friends of the Earth is strongly opposed to S.1758, introduced by Senators Feinstein and Kennedy, and we offer a critique showing that not only does this bill fail to control human cloning, but also that it gives the green light to full-scale commodification of human life.

Environmental organizations are concerned with the accelerated pollution and destruction of wetlands, forests, mountains, agricultural lands, and wildlife which occurred during this past century. Today humanity stands on the brink of a totally new and alarming change in our earth, as well—a change which could carry us into an entirely new realm of artificial existence and a new type of pollution—biological pollution, more ominous possibly than chemical or nuclear pollution. Science now has the capability of creating cloned beings and designer babies and of crossing the species barriers which have for millennia separated plants from animals and some groups of animals from other animals. The real specter of a totally manufactured world is upon us.

The basic environmental case against cloning and engineering of the human germline manipulations (designer babies) is that these actions violate two cornerstone principles of the modern conservation movement: respect for nature and the precautionary principle.

CLONING AND THE PRINCIPLE OF RESPECT FOR NATURE

Environmental organizations embrace an ethic of respect for nature. Environmental organizations carry on a variety of educational activities to help people un-

derstand and appreciate the natural world. Some take people on nature outings, others operate or support nature centers. We strive to demonstrate the interdependence of humans and the natural world and the value of each species' contribution to an entire ecosystem. If a species is altered or wiped out, then changes to the whole ecosystem can be expected.

The very act of cloning animals or people crosses the threshold of respect for the individuality and remarkable features of each species as well as the individuals within species. The principle of respect for nature leads us oppose to the full-scale commodification of nature—whether it be humans, animals, plants, or landscapes.

The push to redesign human beings, animals and plants to meet the commercial goals of a limited number of individuals is fundamentally at odds with the principle of respect for nature. Even though many in the biotechnology business assert that their goal is only curing disease and saving lives, the fact remains that once these cloning and germline technologies are perfected, there are plenty who have publicly avowed to utilize them. Friends of the Earth has even been called upon to debate such people on national television.

Some proponents of human cloning and germline manipulations, for example, extol the virtues of “improving” on the humans, animals, and plants now in the world by re-engineering them. Here is what they are saying:

Lee Silver, molecular biologist at Princeton University, in his book *Remaking Eden: How Cloning and Beyond will Change the Human Family*, envisions a future in which the appearance, cognitive ability, sensory capacity, and life span of our children will become artifacts of genetic manipulation: “The GenRich—who account for 10 percent of the American population—all carry synthetic genes. All aspects of the economy, the media, the entertainment industry, and the knowledge industry are controlled by members of the Gen Rich class—Naturals work as low-paid service providers or as laborers—the GenRich class and the Natural class will become entirely separate species with no ability to cross-breed, and with as much romantic interest in each other as a current human would have for a chimpanzee.”

James Watson, Nobel laureate and co-discoverer of the structure of DNA: “if we could make better human beings by knowing how to add genes, why shouldn't we? What's wrong with it? Evolution can be just damn cruel, and to say that we've got a perfect genome and there's some sanctity to it? I'd just like to know where that idea comes from. It's utter silliness.”

Lester Thurow, noted MIT economist: “biotechnology is inevitably leading to a world in which plants, animals and human beings are going to be partly man-made. . . . Suppose parents could add 30 points to their children's IQ. Wouldn't you want to do it? And if you don't, your child will be the stupidest child in the neighborhood.”

The proposed and ongoing genetic engineering today is radically different from the thousands of years of agriculture where crops and animals have been transformed through cross breeding of very similar species. Experiments in genetic engineering violate the natural species barrier. We have witnessed scientists inserting fish genes in tomatoes and strawberries, making goats which produce spider-like webs in their milk, and adding human genes to pigs.

The cloners like Watson and Silver want to engineer nature to suit their objectives and don't recognize any duties to animals and people who could be redesigned to match the scientists' own vision. There is no reverence or awe of nature but simply a desire to replace plants and animals with the scientists' selection of traits—all for the purpose of making money.

The Feinstein-Kennedy bill (S. 1758) facilitates the objectives of those just quoted because it would allow a completely unregulated commercial industry in human cloning to produce embryos that could be brought to term illegally under a reproductive ban.

To turn next to the practical experience with animal cloning, it is important to note that Ian Wilmut, the developer of the cloned sheep Dolly admits that almost all clones suffer serious abnormalities. The recent finding of premature arthritis in Dolly is one of the strongest indicators to date that there should be, at a minimum, a moratorium on human cloning and on commercial animal production through cloning. What parent wants to risk a child that will be diseased, deformed or developmentally disabled after a few years? Who wants to eat food that may be harmful?

Recent polling shows that 90 percent of Americans do not want human cloning. One of the reasons is that no one should be the subject of an experiment without their consent. Any cloned child would be such an experiment. What Americans do want are therapeutic technologies that do not carry such risks. The *New Scientist* has just reported that a stem cell which can turn into every single tissue in the body has just been found in adults. The article goes on to say: “If so, there would be no need to resort to therapeutic cloning—Nor would you have to genetically engineer

embryonic stem cells to create a one cell fits all' line that does not trigger immune rejection." (January 23, 2002 "Ultimate stem cell discovered" New Scientist)

CLONING VIOLATES THE PRECAUTIONARY PRINCIPLE

The precautionary principle is another pillar of the modern environmental movement. The basic idea of the precautionary principle is that before imposing significant risks on others or society as a whole, we should have a solid grasp of what is being proposed. The principle embodies the wisdom of ancient adages such as "look before you leap" and "an ounce of prevention is worth a pound of cure".

Thus the precautionary principle mandates that when there is a risk of significant health or environmental damage to others or to future generations, and when there is scientific uncertainty as to the nature of that damage or the likelihood of the risk, then decisions should be made so as to prevent such activities from being conducted unless and until scientific evidence shows that the damage will not occur.

A review of major environmental problems of the 20th century reveals a range of unanticipated and awful economic and environmental consequences as a result both of individual actions and various modern technologies. Had the precautionary principle been operative, many of these disastrous consequences might have been avoided. Here are a few examples in the areas of chemicals, civil works projects like dams, introduced exotic species, agriculture, disease and medicine where the precautionary principle was not applied.

The numerous cases of alien, foreign, exotic, or invasive species, which have beset North American ecosystems like a plague in the past hundred years, makes vividly clear the problem of unanticipated consequences. The Federal government estimated that the annual economic costs of invasive species is over \$100 billion. (U.S. Office of Technology Assessment, 1993)

Some introductions of alien species have been deliberate. The starling was brought to America by a man who believed that our country should have all the birds mentioned by Shakespeare. Now starlings are one of the most dominant birds, crowding out native song birds. One of America's most important trees, both from a wildlife and a commercial standpoint, was the chestnut. Very swiftly a disease, introduced through a USDA program, wiped out all the great chestnut trees. No cure has to this date been found. Other invasives like gypsy moths, the Asian long-horned beetle, and Dutch elm disease still plague our forests.

The zebra mussel, which was probably carried in the ballast water of a Black Sea tanker, has proliferated throughout the Great Lakes region and now causes tens of millions of dollars of damage as it clogs up water pipes. A century ago the predatory eel called the lamprey got into the Great Lakes via the Erie and Welland Canals and devastated fisheries and persist to this very day.

The moral of this story is that the ecosystem disruption caused by invasive species not only devastates native flora and fauna but can be enormously costly. Another lesson is that biological pollution proliferates and reproduces and is not easily stopped if it can be stopped at all.

The precautionary principle was not applied when our society began using very dangerous chemicals in the aftermath of World War II. To this very day we have major and costly battles about cleaning up nuclear and toxic waste produced many years ago. A prime example recently in the news is the battle between EPA and General Electric over the chemical PCB waste which still remains in the Hudson River decades after the PCBs were dumped by the company.

Looking at civil works projects, our society did not think through the devastating effect of dams on Atlantic and Pacific salmon and on other fisheries until many decades after precipitous declines in fisheries had occurred. Now dramatic efforts are being made to try to restore some of the salmon runs.

In the area of genetically engineered food, Friends of the Earth exposed the presence in our food supply of genetically engineered Starlink corn, which had been approved for consumption only by animals, not humans. Starlink corn began showing up on grocery shelves all over the country. Despite being planted on only 0.5 percent of the corn field acreage, it contaminated 10 percent of the entire crop in the year 2000.

A decade ago in the case of mad cow disease, the public witnessed the vigorous denial by British officials of any connections between feeding regimes (cows being forced to eat cows) and the disease, and asserted that the disease could not jump from cows to humans. Now they have acknowledged their errors, but the disease has spread to Europe. In other medical news about recent knee surgeries where people have died, the January 20, 2002 New York Times headline reads: "Lack of Oversight in Tissue Donation Raising Concerns—Tight Rules on the Use of Organs Do Not Apply to Tissues". When the subject goes from tissue and organ donations to

the deliberate insertion of inheritable traits, the precautionary principle reminds us that it is not just the patient but future generations who are going to be impacted. One cannot simply recall a bad judgment on inherited traits. That is the lesson of biological pollution presented above.

The great naturalist Aldo Leopold observed that the human role of conqueror is “eventually self-defeating because it is implicit in such a role that the conqueror knows, *ex cathedra*, just what makes the community clock tick, and just what and who is valuable, and what and who is worthless, in community life. It always turns out that he knows neither, and this is why his conquests eventually defeat themselves.” (A Sand County Almanac)

Many scientists and companies in biotechnology are prone to present only the best case scenario. The Friends of the Earth recitation of fiascoes from the past 100 years of biological invasions as well as recent screw-ups in modern medicine show that our society must focus on more than simply best-case scenarios. The precautionary principle poses a direct challenge to uninhibited experimentation on people and the planet—experimentation done in the name of progress, but often driven by the desire to make money. The Feinstein-Kennedy bill does not embrace the precautionary principle but flaunts it.

Senator HARKIN. Thank you very much, Dr. Blackwelder, for your statement, and now we turn to Dr. Maria Michejda, a senior staff associate at the International Center for Interdisciplinary Studies of Immunology at Georgetown University. Dr. Michejda received her M.D. from the Medical Academy in Gdansk, Poland, and is an expert in fetal tissue transplantation and fetal tissue banks.

Dr. Michejda, please proceed with your statement.

**STATEMENT OF DR. MARIA MICHEJDA, SENIOR RESEARCH ADVISOR,
IMMUNOLOGY CENTER, GEORGETOWN UNIVERSITY MEDICAL
CENTER**

Dr. MICHEJDA. Mr. Chairman, honorable Senators, ladies and gentlemen, it is an honor and privilege to present my views on an aspect of the incredibly important issue that you are considering. My name is Maria Michejda. I am a physician involved in research on fetal tissue transplantation. My credentials are in the written testimony.

For over 20 years, my research has focused on the fetal tissue transplantation and on the biology of stem cells from various sources. We initiated the first studies on fetal tissue from second trimester spontaneous abortions over 10 years ago. We found that the stem cells were superior in terms of the biological properties for transplantation, long-term engraftment, and cell reconstitution. Today, I would like to present some of the biological problems of stem cells in the various flavors to you, and to suggest that some of these problems may have disastrous consequences in terms of human therapy. I would like especially to focus on stem cells derived from both reproductive and therapeutic cloning.

Therapeutic cloning is achieved by asexual reproduction methods which involve the so-called somatic cell nuclear transfer, or as we have now, nuclear transplantation. If the transfer is successful, the oocytes containing the implanted genomic material will undergo several divisions to produce a pre-implantation embryo known as the blastocyst, which, after destruction will produce new embryonic cell lines.

In reproductive cloning, on the other hand, the blastocyst is placed in the uterus and may develop into a baby. This has not been accomplished in humans, but many animal examples are known. Both therapeutic and reproductive cloning have the very serious problem of gene imprinting, since all the genetic material

comes from one somatic cell. The consequences of gene imprinting are profound, and affect the very process of cloning, as well as the product of the cloning.

Simply put, the product can be defective. It is now well-appreciated that the nuclear transfer process is highly insufficient, and would be very costly and impractical for therapeutic purposes. Moreover, most clones die before birth during animal reproductive cloning and many survivors display various abnormalities. These include placental and fetal overgrowth, immunological impairment, expressed by autoimmune disease such as the early arthritis diagnosed in the famous Dolly, and accelerated aging.

The consequences of gene imprinting in humans are potentially devastating. Animals may be more tolerant to any genetic aberrations which may initially reside only in the subtle abnormalities. Such abnormalities cannot be ignored in human material, particularly the embryonic cells derived from embryonic cloning and used for transplantation, which would result in the transfer of genetic abnormalities to the recipient. Such aberrations may not be evident at the early stage, but would become expressed at later age. Consequently, cloning technique to acquire stem cells for transplantation are impractical, costly, and may lead to serious medical problems.

Besides major medical problems associated with cloning, one should also take into account the possible legal consequences of professional responsibility and malpractice when something goes wrong.

Finally, there is a limited supply of oocytes suitable for nuclear transfer. This will result in the moral and medical pressure of women of reproductive age. Harvesting of human eggs is not free of dangerous infections, hemorrhage, malignancy, and infertility, which will particularly affect women in financial need.

The initial euphoria associated with the promise of therapeutic cloning has now been tempered by the realization of the multiple problems. This has become evident in the research community, and it is beginning to be expressed into the popular press. While I fully agree with the National Academy of Science panel that more research is needed in the area of stem cells, I would like to point out that the problems associated with human cloning are profound, and cannot be ignored. In fact, this could retard progress in the development of cell therapies, which are in large measure one of the most exciting developments in medicine.

A prohibition of human cloning will not inhibit stem cell research. It will focus attention on proven sources of stem cells such as fetal cord blood, adult cells, and expand the curative potential in scope.

Here, I would like to reemphasize that pluripotent fetal stem cells derived from second trimester spontaneous abortions exhibit proven, highly prophylactic engraftment and curative potential that were made evident in transplantations many years ago. Fetal stem cells have most of the properties of embryonic stem cells, but do not exhibit the uncontrolled replication that is a characteristic of embryonic cells which lead to teratomas, malignancies, and chromosome abnormalities upon transplantation.

PREPARED STATEMENT

In conclusion, technologies for safe and efficient cloning do not exist. Our obligation on the one hand is to protect human life and the safety of patients and, on the other, to prevent dissemination of erroneous information about curative potentials of unproven sources of stem cells for human therapies.

Thank you.

[The statement follows:]

PREPARED STATEMENT MARIA MICHEJDA

Honorable Senators, Ladies and Gentlemen: It is an honor and a privilege to present my views on an aspect of the incredibly important issue that you are considering. My name is Maria Michejda. I am a physician and I have been and continue to be very active in research in the general area of fetal medicine. I am the founder of the Journal of Fetal Diagnosis and Therapy, the principal journal in the rapidly growing field of fetal medicine, and a co-founder of the International Fetal Medicine and Surgery Society. I served as an advisor on fetal issues in a number of academic and non-academic institutions, including the German and Dutch parliaments. Currently, I am an Associate Professor of Radiology and Nuclear Medicine at NYU and a Senior Staff Associate at the Immunology Center of Georgetown University. For over 20 years my main research focus was on fetal tissue transplantation and subsequently on the biology of stem cells derived from various sources, including fetal bone marrow obtained from spontaneous miscarriages, adult bone marrow, cord blood and peripheral blood. We have, in fact, initiated the first studies on fetal tissues from 2nd trimester spontaneous abortions over 10 years ago. As a consequence, we have developed considerable expertise in the acquisition, processing and application of this underutilized and non-controversial source of stem cells (1-8).

My initial studies on fetal tissue transplantation for the in utero treatment of congenital malformations focused on allogeneic transplantation of bone, bone marrow and neural tissue. This work, which was initiated at NIH and subsequently carried out at Georgetown, utilized non-human primates as models resulted in novel techniques for the treatment of neural tube defects in babies before birth. These studies also led to the appreciation of the unique properties of fetal tissue, including cellular regeneration, self-repair, a high rate of cellular proliferation and differentiation, followed by rapid vascularization of the new tissue (6,7). We have focused our attention over the last ten years on the exploitation of the remarkable properties of fetal tissues in general and fetal stem cells in particular (3,4,8).

We have recently conducted extensive comparative studies on properties of stem cells derived from various sources. We examined stem cells derived from adult bone marrow, umbilical cord blood, adult peripheral blood and fetal bone marrow. The fetal bone marrow was, as I said earlier, obtained from 2nd trimester spontaneous miscarriages. Without going into extensive detail, we found that the fetal stem cells were superior in terms of their biological properties for transplantation, long-term engraftment and cellular reconstitution. One of the most important and beneficial characteristics of fetal stem cells derived from the bone marrow is that they are pluripotent and can differentiate into many lineages. They are also highly immature and immuno-incompetent. This means that they are not rejected by the host, in contrast to adult stem cells, and do not induce graft versus host disease. Also, unlike the other sources of stem cells, the fetal stem cells do not require matching of the donor and the recipient (7,9).

Today, I would like to present some of the biological problems of stem cells in their various flavors to you and to suggest that some of these problems may have disastrous consequences in terms of therapy. I would like especially to focus on stem cells derived from both reproductive and therapeutic cloning. Therapeutic cloning is achieved by asexual reproduction methods, which involve the so-called somatic cell nuclear transfer. This is accomplished by microinjection of the nucleus from a human donor cell that carries a complete set of chromosomes into a human ovum from which the nucleus has been removed. If the transfer is successful the oocyte containing the implanted genomic material will undergo several divisions to produce a preimplantation embryo known as the blastocyst. After five days, this entity is composed of 100-150 embryonic cells. It is then destroyed in order to create new embryonic cell lines in culture. In reproductive cloning on the other hand, the blastocyst is placed in the uterus and may develop into a baby. This has not been accomplished in humans but many animal examples are known (10-12).

Both therapeutic and reproductive cloning have the very serious problem of gene imprinting since all the genetic material comes from one somatic cell. The consequences of gene imprinting are profound and affect the very process of cloning as well as the product of the cloning (10,11). Simply put, the product can be defective. It is now well appreciated that the nuclear transfer process is highly inefficient and would be prohibitively costly and impractical for therapeutic purposes. Moreover, most clones die before birth during animal reproductive cloning and many survivors display various abnormalities. These include placental and fetal overgrowth, immunologic impairments, expressed by autoimmune diseases (such as the early arthritis diagnosed in the famous Dolly), and accelerated aging. The consequences of gene imprinting in humans are potentially devastating. Animals may be more tolerant to epigenetic aberrations, which may initially result in only subtle abnormalities. Such abnormalities cannot be ignored in human materials, particularly in embryonic cells derived from therapeutic cloning and used for transplantation, which could result in the transfer of the abnormalities to the recipient, the experiments in mice notwithstanding. Such aberrations may not be evident at early stages but would become expressed at a later age. Consequently, cloning techniques to acquire stem cells for transplantation are impractical, costly and may lead to serious medical problems.

Besides the major ethical and medical problems associated with cloning, one should also take into account the possible legal consequences of professional responsibility and malpractice when something goes wrong. Finally, there is a limited supply of oocytes suitable for nuclear transfer. This will result in moral and medical pressures on women of reproductive age. Harvesting of human eggs is not free of dangers of infection, hemorrhage, malignancy and infertility, which will particularly affect women in financial need.

The initial euphoria associated with the promise of therapeutic cloning has now been tempered by the realization of the multiple problems. This has become evident in the research community and is beginning to be expressed in the popular press (see New York Times, Dec. 18, 2001). While I fully agree with the National Academy of Sciences panel that more research is needed in the area of stem cells, I would like to point out that the problems associated with human cloning are profound and cannot be ignored. In fact, this could retard progress in the development of cellular therapies, which are in large measure one of the most exciting developments in medicine. A prohibition of human cloning will not inhibit stem cell research, but will focus attention on proven sources of stem cells such as fetal, cord blood, and adult cells and expand their curative scope. Here, I would like to re-emphasize that pluripotent fetal stem cells derived from 2nd trimester spontaneous abortions exhibit proven highly proliferative engraftment and curative potentials that were made evident in transplantations many years ago (13–24). Fetal stem cells have most of the properties of embryonic stem cells but do not exhibit the uncontrolled replication that is a characteristic of the embryonic cells, which leads to teratomas, malignancies and chromosomal mosaicism upon transplantation.

In conclusion, technologies for safe and efficient cloning do not exist. Our obligation on one hand is to protect human life and the safety of patients, and on the other to prevent the dissemination of erroneous information about curative potentials of unproven sources of stem cells for human therapies.

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Senator HARKIN. Dr. Michejda, thank you very much.

My personal thanks to all of the panel for being here today and for all of the work that you have done in the past in focusing on this issue. It is one that is contentious. We all know that, and there are views on different sides. Some of the views are different based on medicine approaches, some of the views that differ are based upon ethical considerations, some of the views differ based on fundamental religious beliefs.

So you have a confluence here not just on the medical differences, but ethical and religious differences on this approach, and as you might expect, the Congress of the United States is now being asked to step in—not being asked, I guess Congressmen and Senators are stepping into this fray, as well as the administrative end of the Government, the executive branch. Again, I am not a scientist. I have no expertise in this area. I study, I read as much as I can comprehend, but we are trying to figure a way to try to thread this needle, so to speak, on where we can keep the research moving ahead, but to do it in a manner that, while it may not satisfy every person's ethical problems, will at least answer the majority of them.

I mean, there are people with certain beliefs, deeply held, which I respect, that are opposed to many of the things we have as commonplace today in medicine, and after all, there are members of

the Christian Science religion who do not believe in any kind of medical procedures. I respect that. That is their belief, but again we have to move ahead and try to figure out what we can do in the framework of a free and open society, paying attention to being cognizant of and respectful of these ethical differences and religious differences.

Now, when it comes to cloning questions, as I said before, it seems like everyone here, it seems to me, agrees that human cloning should be banned. Now, I use my chart here. I point to it again. I used it last fall. I do not think it has changed since then. We have got two courses here. Correct me if anything is wrong on this chart, but you take DNA from a sick patient, you take a donated egg, you take out the DNA of the egg, you put in the DNA of the sick patient, then you have two courses of ways you can go. You can go to implantation, to have a cloned human, or you can go down this way on cellular transfer and develop the blastocyst and the stem cells, and then the stem cells later on to cure the patient.

There are some who want to ban this procedure. The bill that Senator Specter and I introduced today puts the ban on human cloning. It would permit cellular transfer but not implantation, and the bill we introduced has both civil penalties and criminal penalties for engaging in that activity.

Is that, Dr. Weissman, sort of what your bioethics panel suggested?

Dr. WEISSMAN. First, we are not a bioethics panel. We are the scientific panel.

Senator HARKIN. You are right, you did not get into ethics.

Dr. WEISSMAN. You are absolutely correct, and I think it is really important that our recommendation said that there be a legally enforceable ban for human reproductive cloning. That would end any speculation that somebody, some mad scientist in the lab would take the incipient stem cells in their earliest stages that one wants to study to use to make stem cell lines and put them in a uterus. There is a legally enforceable ban that you put in to protect against that possibility, and I think that is sufficient. You do not need to go further than say, if you try to practice reproductive cloning with these cells, or in the attempt to make a blastocyst to make these cells, you will be subject to a legally enforceable ban.

Senator HARKIN. Well, here is the dividing line. Dr. Blackwelder, what is wrong with that approach?

Dr. BLACKWELDER. Well, the basic point is that you may try to put it there, but the problem is that we have seen all too often things do not work.

For example, the anthrax, it was reported in the paper from Fort Dietrich, disappeared, something that should have been off-limits. It got loose. So what happens with the rogue scientists and so forth, they get free, and we move forward in this direction.

I do not know what your bill is going to say, but the Feinstein-Kennedy bill did not tighten the loopholes in this regard, and the critique we have provided demonstrates a number of ways in which there is not even a review body on it, so I cannot comment on what your bill is going to do, but that bill is too much like a Swiss

cheese, and once you start down that direction, you see, with this going, where do you draw the line?

The question we raise also, isn't there enough that can be done on the promise of stem cells—just in my testimony I quoted the article from the *New Scientist* yesterday. They found a cell in adults that may turn into every single tissue in the body. This might essentially preempt the whole debate if this is true. A lot of checking has to be done.

That is why we suggest that a moratorium on this, so we do not risk the down side but allow the medical promise to be explored. We are just at the early stages. Why do we have to go the very risky route, and a route that the attempt by some of your colleagues in their bill would surely not foreclose.

Senator HARKIN. Well, there is a difference between our bill and Kennedy's bill. I do not need to go into that right now. We put in criminal penalties as well as civil, plus ours is the total ban. I think that is where we differ from you. You wanted a 5-year to look at it. We just banned it outright, so there are some differences there.

But this question, well, they found a new cell that may—I do not know all about that, but I will ask Dr. Weissman to comment on that.

Dr. WEISSMAN. Sir, one thing that is important that everyone understand about science is that in our spirit of free inquiry we do experiments, and we publish experiments, and they are published in peer review journals, meaning people try to look at it to make sure they are correct, but it is not far enough to do an experiment that looks correct from one point of view at that time by one group. You have to have independently reproduced experiments.

The article in the *New Scientist*—I have not read it, but I know what it is about—does not come from a paper that is published in a peer review journal, much less independently verified. It would be great if what is in the *New Scientist* turns out to be true. It does not affect the issues at all that we are trying to get at.

We have to understand that nuclear transplantation to create stem cells allows us for the first time to try to understand not only how to transplant stem cells and to transplant cells, therapeutic cloning, which I think everybody is focused on, but much more importantly, opens up an area of research we have not been able to pursue, and I will give you a perfectly clear example, I hope.

Many of us, probably everybody in this room, carries genes that give you a risk to inherit a particular disease, whether it is cardiovascular disease, heart attack, stroke, cancer development, Lou Gehrig's disease, Parkinson's disease, whatever, so those are genetic factors that make a risk, but not everybody with those genetic factors get that disease.

But in those people who get the disease, they have got the genetic factors combined in them in a way we still do not understand, but it leads to the disease, so if we can take the nucleus of a cell from that patient, or even more importantly the nucleus of the diseased cell from that patient and create a cell line that we can study in test tubes, in the mature cells, in mouse models, it opens up an incredible avenue of research. It is so general and so pervasive that

it will affect all of the kinds of research that we do as biomedical scientists.

And I will remind you that this kind of a debate went on about 20 years ago when a number of groups thought putting together two pieces of DNA, so called recombinant DNA, was creating life, but we now have many drugs, erythropoietin, the interferons, growth hormones, GCSF and so on, which are actual and real, practical therapies. Hundreds of thousands of lives, conservatively, are saved or made better every year in the United States.

Had we banned that research because of a precautionary principle those lives would not exist today, and we would not have a biotechnology industry which helps us move forward.

Senator HARKIN. Dr. Weissman, my time is up. I will get to my second round. I will turn to Senator Specter.

Senator SPECTER. Thank you, Mr. Chairman.

Dr. Michejda, I have great respect for the work which you have done in fetal tissue, and the moral issues relating to these subjects, and if the embryos could produce life, I believe that is what we ought to use the embryos for, every last one of them, to the extent that they can produce life.

In the bill which Senator Harkin and I worked on this year, we took a start with \$1 million on a fund to promote adoptions, and People Magazine has a very interesting article in the January 24 issue on Last Chance Family on adoptions, and we are now working on tax credits to encourage adoptions, but there is no doubt that however many adoptions there may be, that there will be embryos left over. In vitro fertilization creates more than are needed, even with a mammoth program on adoption, so the moral question comes up, if these embryos can be used for stem cells to save lives, isn't that a morally acceptable use, contrasted with throwing them away?

Dr. MICHEJDA. Your Honor, I think it is here what we discuss is not the moral aspect but medical aspect and feasibility of that technology to apply in future cellular therapies, and that is what that important medicine, that is the future of medicine, practically.

Obviously, the sources are very important, and safety of these sources in transplantation for the patients, for the transmission of possible——

Senator SPECTER. When you talk about safety, I want to talk about that in a minute, but just on the strict moral issue, if the embryo is going to be thrown away, is it immoral to use it to save lives? If the embryo can create a life, I agree it is immoral not to do that, but if the embryo is going to be thrown away, is it immoral to use it?

Dr. MICHEJDA. You ask me for moral and ethical questions, and I am here as a physician to answer the medical problems associated with the cloning. I would like to stress again that both, at least in my opinion, reproductive and therapeutic cloning has to be done at initially the same fashion, the same way, and carries the same problems and consequences as far as the transfer of some disastrous diseases, or immunological deficiencies, yes.

Now, if we are talking about the problems of embryo, or cells which are existing, and I have to say that what I know from col-

leagues in the IV centers, the number of cells, stored cells, is very small, and decreasing, simply because technology improved.

Finally, this technology was taken from animal husbandry. Now it is improving.

Senator SPECTER. Pardon me, I have a very limited amount of time. Let me ask one question on your statement about abnormalities.

Dr. MICHEJDA. Yes.

Senator SPECTER. I notice that your line of expertise is on fetal tissue. Can you document abnormalities resulting from nuclear transplantation? Do you know of actual cases where there have been abnormalities?

Dr. MICHEJDA. It was never done in humans, but there is literature on animals about problems associated with this technology, so it exists.

Senator SPECTER. Do you have examples on abnormalities from animals, on nuclear transplantation?

Dr. MICHEJDA. Yes. There is overgrowth, there is a significant skeletal malformation, there is accelerated aging, and the last reports on the famous Dolly, which has arthritis. Obviously, there is a certain—the problem of autoimmune diseases is very real in such a situation, when you have one cell donor and recipient, actually.

Senator SPECTER. Dr. Michejda, to the extent you can provide the subcommittee with specifics on abnormalities, we would appreciate it. I had asked you the question on morality because your resume, your curriculum vitae, expressed that aspect of your work, but I respect your answer there.

Dr. MICHEJDA. The references regarding animal experiments are listed and will be on the record.

Senator SPECTER. Okay. Thank you very much.

Dr. Blackwelder, I agree with a great deal of what you have said. We have had a terrible problem in Lake Erie with beaver mussels, and I ought to take a look at that chestnut blight on our Agriculture Subcommittee on Appropriations, and I certainly would not want to commodify all types of life on earth, but that does not point yet to the issue of nuclear transplantation. We are not going to create a designer baby or a commodity. We are going to take a woman, for example, who has Parkinson's and we are going to have a procedure where her DNA is going to be part of the production of the stem cell to save her life.

Now, isn't that something where you draw that kind of a line, which we are prepared to do very forcefully in the legislation, and put up a wall, like Jefferson's wall, a separation of church and State. Is that not something which is acceptable?

Dr. BLACKWELDER. See, you are outlining a best-case scenario. You are doing something, and whatever changes are done, the patient may improve or may not, but it does not affect others or society as a whole.

What we are saying is that we are on the edge of something even much bigger than that, because you go right from the issue of cloning to inheritable traits, designer babies and so forth, and the questions have to be asked, are any things being done here that are actually going to lead to the insertion of genes that are passed

on, because once you start passing things on, you cannot blow the whistle and say, oops, we have made a mistake.

This is a form of biological pollution. It is unlike chemical pollution, or nuclear radioactive pollution. Those decay and wane over time, but we have seen with the examples that I cited, you have got things out there replicating and so forth. That is why we are saying, incredible oversight needs to be provided here. We need to know more clearly what is going on.

The Feinstein bill did not do it. The Feinstein bill did not even provide any regulatory scheme about women possibly selling their eggs, the patenting of the cloning embryos and everything else that could sort of set up these kind of workshop mentality. What is actually going to go on here is a big issue, and it is beyond the kind of case that you just outlined. I am just trying to draw out for the committee the larger, overarching issues that need very extensive discussion.

Senator SPECTER. Oh, I understand your testimony. You are saying the case I outlined is acceptable so long as it does not lead to reproductive cloning.

Dr. BLACKWELDER. Well, for example, if you are using a discarded embryo, okay, and stem cells from that, or adult stem cells, or stem cells, if this article I cited, it turns out that works, Friends of the Earth does not have a problem with that, okay, but if you are starting out with the same kind of situation where you are going to, under certain scenarios of screw-ups and so forth, move forward and inadvertently, or clandestinely, or criminally things happen—for example, under the Feinstein bill, what is to stop some people from taking those—you are right at your middle stage, and you go over to a foreign entity, and they start the cloning process.

Senator SPECTER. My time is up, so I am going to on the second round ask Dr. Jaenisch and Dr. Weissman questions, but I am going to suggest to Senator Feinstein that she call you when she has her hearing, because you have done more testifying about the Feinstein bill than anything else, and I am very interested in that, but not as interested as she is.

Dr. BLACKWELDER. Well, I just hope you will not—I mean that I hope your legislation is not going to repeat some of the defects.

Senator SPECTER. You have practically convinced me to vote against the Feinstein bill and I do not know anything about it.

But I would terminate with your point that if we stop there, your testimony was it is okay with Friends of the Earth. Well, I am a friend of the earth myself, and we are going to stop right there. We are not going to take that step beyond.

I would like to come back on round two with you, Mr. Chairman.

Senator HARKIN. Thank you. I think Dr. Jaenisch wants to respond.

Dr. JAENISCH. Yes. I would like to respond to some scientific issues which were raised by Dr. Michejda about the concern that problems could arise in using cloned embryonic stem cells, and imprinting was mentioned as being one of the problems.

Now, my laboratory is working with imprinting for the last 15 years, so let me clarify these issues because I think there is some confusion here.

I think it is right, the most serious abnormalities in cloned animals are called by what we call faulty reprogramming, or it is a faulty expression of these imprinted genes which are important for the development of the whole embryo.

In contrast, when an embryonic stem cell is differentiated into muscle cells, nerve cells, cells of the pancreas, then these functional cells are derived without going through an embryonic stage. There is no embryo, there is no heart development, so these streams are not important. So to summarize, the faithful expression of an imprinted gene is crucial for embryonic development, but has probably little function for the adult cell.

Of course, in cloning, and I think that is what she was referring to, in cloning you ask one nucleus to give rise to every tissue of the animal, including going through all development. This is a big problem. In embryonic stem cells there is no embryo made, so these genes are not called into action. They are not important.

So let me just emphasize, I think, the very important difference here. In cloning, the donor nucleus must direct development of the whole embryo, with all organs, and there are a serious abnormalities we see in every cloned animal, as I have stated. This is not the case in tissue—so then we have found that embryonic stem cells themselves are unstable, which raises concerns there might be problems in transplantation.

Now, there is extensive experience from the last 20 years with mouse embryonic stem cells. There is not a single case where transplantation of an embryonic stem cell derivative into a mouse has caused any abnormalities. There is not a single case, because—I should say transplantation of embryonic stem cells in a developing embryo to form a so-called chimeric mouse, which is a mouse which is composed of cells which come from a fertilized embryo and from the stem cell, in this case there is no abnormality.

Senator HARKIN. Let me make sure I understand what you have just said. In however many—you say 20 years, or 15 years of doing this research—that if you take a stem cell—are we talking about embryonic stem cells?

Dr. JAENISCH. Embryonic stem cells.

Senator HARKIN. An embryonic stem cell, and you place it in an egg whose DNA has been removed and let that develop into the embryonic stage, that there are abnormalities in almost every case.

Dr. JAENISCH. If you ask this nucleus to develop into an animal.

Senator HARKIN. That is what I am talking about.

Dr. JAENISCH. Yes.

Senator HARKIN. If it goes beyond the embryonic stage.

Dr. JAENISCH. Yes.

Senator HARKIN. If, however, you take those cells at the blastocyst stage and remove those stem cells, and let those stem cells develop and multiply, and then take those stem cells and implant them in a mouse, for example, that you say there is no case, not one, in which it has expressed itself as some abnormality.

Dr. JAENISCH. That is correct. This is a very stringent experiment, because in this case you put the stem cell into the early developing embryo, so it is has to contribute to all tissues.

Senator HARKIN. Yes.

Dr. JAENISCH. But the presence of the normal cells, the normal cells being from the fertilized embryo, from the host embryo, totally then corrects the problems the stem cell would do if it was alone.

Senator HARKIN. Let me ask this question. In these experiments, are those stem cells, the stem cells that were later placed in the animal, in the mouse, were those embryonic stem cells derived from that same mouse, or from other mice?

Dr. JAENISCH. Can be from another mouse, from any mouse.

Senator HARKIN. From any mouse?

Dr. JAENISCH. They can be also derived from a cloned embryo. It has been shown, even if they were derived from a cloned embryo, the so-called chimeric mouse which develops is totally normal, so the problems we see in cloning do not apply to stem cells which give rise to differentiated cells in culture, because the genes we know, which are very important for—

Senator HARKIN. But tell me, in your own words again, tell me why it is that if you take the stem cells and let them develop into the embryonic stage and beyond, that there are abnormalities, but if you take those stem cells in the blastocyst stage and remove them, and let them multiply on their own as stem cells, why are there not any abnormalities there? I do not understand. Is there any reason?

Dr. JAENISCH. Yes, I think there is a logic behind this. The logic is that when you take embryonic stem cells and culture them in the Petri dish, and derive, let us say, nerve cells, then you do not have to go to embryonic development, so the genes which are a problem do not have to be correctly expressed. They are not needed, and these genes which have to be correctly expressed to make an animal are not important for the function of the nerve cell or the beta cell once it has been derived. You can derive this in culture.

So when you take those cells and transplant them into a patient, for example, or into a mouse, they function perfectly well. It does not matter that the expression of the genes is not correct, the ones that are needed for the very early stages of development, because you do not need early stages of development for this type of approach, so there is a basic difference here.

Senator HARKIN. We both have to call this to an end, but I just want to ask one question of all the panelists. I will start with Dr. Michejda.

Dr. Michejda, do you support in vitro fertilization?

Dr. MICHEJDA. As what, as a technology?

Senator HARKIN. No, I mean people right now, infertile couples right now sometimes will go to in vitro fertilization and then take that and implant that in the woman's womb, and then it develops into a baby. We have been doing that for years now. I just wondered, are you supportive of that, or not?

Dr. MICHEJDA. There are several types of in vitro fertilization, and there is one form where the surrogacy is not used. In other words, this is between the couple, the exchange of semen and ovum, so I think that is acceptable. If we go to some surrogacy and get from different donors, not partners and so on, we have a lot of legal problems and ethical, so I would be definitely against this.

Senator HARKIN. But if you had a woman and a man who wanted to have a child, but for some reason were incapable, but the woman produced eggs and you could remove the egg and take the sperm from the man, and combine those in a Petri dish and then take that and plant that in the womb for the reproduction of a child, you say that is okay.

Dr. MICHEJDA. Well, as long as it is within family.

Senator HARKIN. Well, now you are getting into moral and ethical issues. I am just talking about medical issues.

Dr. MICHEJDA. No, legal, mostly legal, because there were many problems.

Senator HARKIN. But you say that is okay.

Dr. MICHEJDA. I would say yes.

Senator HARKIN. How about you, Dr. Blackwelder?

Dr. BLACKWELDER. We have not taken a position on that, but I want to reemphasize in my testimony that we are not only opposed to reproductive cloning, we want a moratorium on the therapeutic cloning.

Senator HARKIN. You want to stop it all?

Dr. BLACKWELDER. A moratorium for 5 years. We are not opposed to stem cells. We say stem cells have a lot of promise, but there may be other ways to get them, other things to check out.

Senator HARKIN. So you are opposed to embryonic stem cells.

Dr. BLACKWELDER. Yes.

Senator HARKIN. You are okay with adult stem cells. You are okay with that.

Dr. BLACKWELDER. Yes. Yes, or if an embryo is discarded, if an embryo is discarded, going to be thrown away, then that does not raise all the problems that we have tried to lay out, whereas if you turn women into egg factories, the commodification or patenting of life, and the other issues relating to inheritable genetic traits.

So if you understand, I want to be very clear I have laid it out, we should place that moratorium on what we call the therapeutic cloning for 5 years.

Senator SPECTER. With respect to the moratorium, Dr. Weissman, let me thank you for the work which your panel has done, the telephone conversation which you and I had back in August and your work generally. Dr. Burt Vogelstein from Johns Hopkins has given us a list of the potential of stem cells, and this goes to the heart of the issue of a moratorium, whether we ought to be doing the work here, notwithstanding the fact that if we stop nuclear transplants the work will go all around the world, where the research is being undertaken.

Dr. Vogelstein produced this list for the utility of stem cells: cardiovascular disease, 58 million; autoimmune disease, 30 million; diabetes, 16 million; osteoporosis, 10 million; cancers, 8,200,000; Alzheimer's, 5,500,000; Parkinson's 5,500,000; spinal cord injuries, 250,000; birth defects, 150,000, with a conservative estimate that there would be a saving of 1,700,000 lives each year, on the potential for stem cell research and the nuclear transplants, and that is why I categorized it as a life and death matter. I would like your evaluation as to the importance of stem cell research and nuclear transplants in terms of saving 1,700,000 a year, going to the issue

of moratorium and the sense of urgency which I believe we need here.

Dr. WEISSMAN. Sure, so the first point is that anybody who would enact a moratorium closes the window of possibility of therapy for those people who have the disease, so there is no middle ground here. If you have a ban or a moratorium on that kind of research, you are really in the situation that you are going to prevent therapies from development.

Now, science is unpredictable, so we cannot say the exact time at which all of these valuable things will come out. I can just say that this is as fundamental as recombinant DNA, and unpredictably that led to great therapies, and very rapidly under the guidance and the control of the Recombinant Advisory Committee.

There is no doubt that we want, as a community, to have the usual kinds of safeguards of human subject research and tissues from humans going through institutional research boards and other boards like a national panel, but I agree with you entirely that the medical potential for this is broad, because it really affects almost every disease that has at least a genetic component to it, or where tissues degenerate that are important, like in Parkinson's or Lou Gehrig's disease.

Senator SPECTER. Thank you very much. This has been a very excellent panel, Mr. Chairman. I thank you all for your contribution. Thank you.

Senator HARKIN. Thank you, Senator Specter.

I, in closing, just want to note Dr. Weissman's comments about the drugs that have been developed and the lives saved because we did not close the door on recombinant DNA research. I think my environmental record is pretty good in terms of where Friends of the Earth are situated and things like that, but again, we all want to be precautionary. We all want to proceed with caution.

Shutting a door is not precautionary. It is opening the door, but doing it very carefully, doing it under guidelines, doing it under the strictest of peer review, and yes, ethical guidelines, to be sure, but to open it carefully, not just to slam it open, but to open it carefully, to look behind that door and see what is there. That is precaution. That is precaution.

To say somehow that we should have a ban, I say to my friend Brent Blackwelder, or to put a moratorium on it—go out and talk to people with Parkinson's disease and tell them they have got to wait some more. You go talk to my nephew, who has been quadriplegic for 20 years with a spinal cord injury, who keeps up on this daily. He knows exactly what is going on out there, and he knows what has been happening in rats in terms of spinal cord rehabilitation through stem cells. Tell him to wait because you have a little bit of concern here, there has got to be a moratorium. You know, the old Native American adage, you know, walk a mile in the moccasins.

There are a lot of people out there with suffering that can be alleviated. We do not know when. We do not know if any of it is going to work, but to shut the door on it, and to say we are going to have a moratorium I think is just—I am sorry, that is where I depart. Precaution, yes. Open the door carefully, yes. Have a care and concern for moral and ethical considerations, yes, and try to

find some way of moving ahead under those kinds of guidelines, and that is what this committee and what others here are trying to do.

I fully recognize there are the extremes. There are those that say, there should not be any controls. There are those that want to clone human beings right now. There are some crazies out there right now that want to clone human beings. They want to be the first to do it.

And there are those on the other side that do not want anything. There are some out there opposed to all biotechnology. Nothing, stop it all.

Somewhere between, we have got to chart a course.

Dr. BLACKWELDER. Yes, well, why not exhaust the adult stem cell possibilities first?

Senator HARKIN. Well, I answer you this way. Basic research, I have often said, is like—you have got 10 doors out there. We are going back to the door analogy. Basic research is saying, what is behind those doors?

Well, if you open one of the 10 doors, chances are you may not find the answer. If you open half of the doors, you have got a better chance of finding the answer. If you open 9 of the 10 doors, you have got a really good chance at finding the answer. I do not want to stop adult stem cell research. Let it go forward, but do not stop embryonic stem cell research, because we do not really know right now which is going to have the most promise, so that is all I am saying. Keep them both going, but do it under these guidelines.

Dr. Michejda, I am going to let you have the last word here, and then I am going to close.

Dr. MICHEJDA. Thank you very much. Two problems. First of all, we are talking about therapies, which means a lot of cells, a lot of embryonic cells from cloning or from in vitro fertilization. The fact is, which I tried to explain with Senator Specter, that we do not have unlimited sources of cells.

Senator HARKIN. We do not have unlimited—

Dr. MICHEJDA. Unlimited sources of cells for cloning or whatever, and at this point the whole burden really is on the reproductive system of women.

Senator HARKIN. But wait, we do have nearly an unlimited source because we have thousands of embryos that are now frozen in nitrogen left over from in vitro fertilization that are going to be destroyed.

Dr. MICHEJDA. There are not so many, Senator. I mean, a thousand.

Senator HARKIN. There are several hundred that I know of anyway.

Dr. MICHEJDA. Well, but that is not therapy. That is not enough.

Senator HARKIN. But every scientist I have ever talked to said that within that universe out there of leftover embryos from in vitro fertilization, there is more than ample supply of stem cell lines.

Dr. MICHEJDA. We are talking here about approval or rejection of cloning, as such, as the source of cells for therapies for the future, therapies in this country or in the world. I want to say again, the sources are limited for that massive therapies in the future.

For research, obviously, probably not, and not all of the cell lines are good, and we know about it.

So anyway, we have to face some crisis somewhere, and this will depend upon the reproductive system of women, and stimulation, and getting more cells. I am looking more beyond today. I am thinking about the future.

Now, also, as far as the gene imprinting in animals is concerned, there are many reports of abnormalities. In fact, in Germany, the ban of cloning was based on the facts which were observed in the log-ins, and the reports were in Science, and I am serving as advisor to the German parliament on fetal issues, and I am more or less informed that that is the situation.

Senator HARKIN. I have just been told that there are over 100,000 frozen embryos in England alone, 100,000, and I would submit that with that kind of universe out there, the cell lines that you would need are more than adequate for the kind of research that needs to be done.

Dr. MICHEJDA. Research, yes, but not therapy.

Senator HARKIN. I need to close this up, with respect to——

Dr. WEISSMAN. I am not going to go to that issue. I just wanted to correct something you said, or I do not think I was clear enough in saying to you. The National Academy's recommendation did not say the ban should just last 5 years. It said the scientific and medical issues should be relooked at within 5 years, because we need to give Congress bioethics panel an update on what we know.

Senator HARKIN. Fair enough. Fair enough.

Well, it has been a very good panel, and obviously you are all very bright and capable and very learned individuals, and again we invite you to continue to give us the benefit of your thoughts and your advice as we move ahead in this area. We have a job to do, and we are going to have to do it.

SUBCOMMITTEE RECESS

Thank you all very much for being here, that concludes our hearing.

[Whereupon, at 12:25 p.m., Thursday, January 24, the subcommittee was recessed, to reconvene subject to the call of the Chair.]

CLONING, 2002

TUESDAY, MARCH 12, 2002

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN
SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 2:04 p.m., in room SD-192, Dirksen Senate Office Building, Hon. Arlen Specter, presiding.
Present: Senator Specter.

PROHIBITING HUMAN REPRODUCTIVE CLONING AND SAVING MEDICAL RESEARCH

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. The Subcommittee on Labor, Health and Human Services and Education will now proceed.

We regret the shift on the schedule, but after this hearing was set, President Bush announced his intention to travel to Philadelphia this morning, and when the President comes to Philadelphia, that is a command performance for those of us who represent Pennsylvania. We thank the staff for rearranging the schedule, and we thank all the witnesses for rearranging their schedules to accommodate this change in timing.

The chairman of the subcommittee, Senator Harkin, is very heavily engaged in the agriculture bill, so he is going to be unable to join us. But he has been a leader on the issue of NIH funding and stem cells and nuclear transplantation, which some call therapeutic cloning as a misnomer.

We are very appreciative to have with us a former Senator, Connie Mack, who was the original sponsor of the resolution to double the NIH funding over a 5-year period. That has been the rallying call for an increase in funding for NIH, some \$12 billion a few budget periods ago to now \$23 billion.

At the outset, when we set on the course, this subcommittee took the initiative in asking the Budget Committee for \$1 billion, and we were turned down. So, we went to the floor, had a vote, lost 63 to 37, but found the billion dollars as a matter of priorities in other matters.

And then having been turned down on \$1 billion, we asked the next year for \$2 billion, which is the way appropriations work. We were again turned down, but found the money on reassessing priorities. On the last vote, it was 96 to 4 in favor of increased funding for NIH.

This year the President has asked for \$3.7 billion more for the National Institutes of Health, which is a tribute to President Bush, and to his administration. It shows how popular the program has become and how much public acceptance it has had.

In November 1998, stem cells burst upon the scene, and this subcommittee promptly scheduled a hearing and has now had 12 hearings on the subject. We have found, as many of you, if not all of you, an ideological divide. The embryos which produce the stem cells also produce life, but many of them are discarded. Up to 2 dozen are created for in vitro fertilization and approximately 6 or 8 are discarded. Many of us think that rather than throw them away, they ought to be used to save lives.

The subcommittee put \$1 million in the 2002 budget to stimulate adoption of embryos. If they could all be adopted, that would be wonderful, then we would not have any left over for stem cells. But that will never happen because there are tens of thousands of them which will not be used. And we are currently considering legislation for a tax credit, up to \$5,000 for people who adopt an embryo for a child born through that process.

We are now involved in another controversy over so-called therapeutic cloning, which is not cloning at all. There is a consensus not to make another individual, not to make another Arlen Specter, for example. If we could make another Kevin Kline, it might be another matter. But the so-called therapeutic cloning, as I say, is not cloning. What it involves for example, is taking a cell from somebody who has Parkinson's, taking an egg, removing the DNA, putting that cell in the egg, and then the stem cells, which are produced, are not rejected.

We are about to have a Senate debate on the subject in the next several weeks, and there is a real need for public understanding and a public debate if we are to win that vote. This is very critical.

We have Congressman Bart Stupak scheduled to testify, who has a different view than Senator Connie Mack. Senator Mack's testimony we believe is especially important because he has a strong pro-life record, as do other Senators, and in that context, Senator Hatch, who has been a strong proponent of stem cells, has not yet taken a position on nuclear transplants. Senator Gordon Smith has taken a position in favor of stem cells and nuclear transplants, and we have many Senators who have come over to our side in supporting stem cell research. Some 64 signed letters last spring and 12 more favored a broader Federal role on Federal funding on stem cells. And then the President made his announcement on August 9 permitting Federal funding for stem cell lines in existence at that time. It is an issue which has been put on the back burner after 9/11. But the so-called therapeutic cloning issue is very much before us now.

So, with that introduction, I am delighted to turn to my distinguished colleague, Senator Mack. Senator Mack served in the House of Representatives, and in the U.S. Senate for two terms. And we have conducted this introduction long enough to allow Congressman Stupak to arrive to hear the beginning of Senator Mack's testimony. Connie, the floor is yours.

STATEMENT OF HON. CONNIE MACK, FORMER U.S. SENATOR FROM FLORIDA

Senator MACK. Thank you, Senator Specter. I am particularly pleased to be back before the subcommittee. As you know, I served on this committee a few years ago. I am delighted to be with you.

Actually before I begin my testimony on the subject of today's hearing, let me commend and thank you, Senator Harkin, and the other members of the committee for the bipartisan effort to achieve the goal of double funding of the National Institutes of Health. With your continued leadership, this historic effort will be completed in the fiscal year 2003. I am convinced that we will continue to see significant advances in science and medicine for many generations to come as a direct result of the basic clinical research that has been conducted during this 5-year period.

This marks the first time since I retired from the Senate that I have testified before my former colleagues. But I feel so strongly about the policy that the Congress of the United States might actually criminalize important biomedical research that I have to speak out, and I appreciate the opportunity to do so.

As you may be aware, one of my main areas of interest and where my passion truly lies is biomedical research. Today I am involved with several biomedical research entities precisely so I can help make a difference in advancing this important effort.

The U.S. Senate will soon act on legislation already passed by the House of Representatives that would ban an important area of medical research that holds great promise for millions of patients who suffer from medical conditions such as heart disease, spinal cord injury, and diabetes. The legislation would criminalize the research and prohibit any therapies from entering our country that were produced as a result of this research, even if the therapies are proven to be safe and effective.

The idea that Congress would make criminals of researchers pursuing cures for diseases that kill and debilitate our loved ones is almost unimaginable. But if the Senate passes this controversial legislation, that is exactly what will happen.

What is this research? As you know and as you indicated earlier, it is called somatic cell nuclear transfer, or SCNT, research. SCNT is the ability to derive a patient's own stem cells, which are the building blocks of human development, and use those stem cells to repair the patient's damaged cells or tissues.

The research is sometimes referred to as cloning, but all cloning is not the same. One type, which most believe should be stopped, is the cloning of humans. It is called reproductive cloning. But there is another type called therapeutic cloning which could be used to replace damaged cells and tissues. SCNT research is an example of therapeutic cloning and is the type of research that some want to criminalize.

Let me be clear. Like most Americans, I oppose human reproductive cloning. It is dangerous and raises far too many moral, ethical, and legal issues and could have enormous social implications. That is not what this debate should be about.

It is important to make the clear distinction between reproductive and therapeutic cloning. For therapeutic purposes, scientists

use a technique that I mentioned a moment ago called somatic cell nuclear transfer, or SCNT.

How does it work? First, the nucleus of an egg cell is removed. In its place, researchers insert the nucleus of an already differentiated cell, a cell that performs a specific function in the body. Chemicals are added to stimulate the egg to start dividing. This egg cell is never fertilized by sperm and will never be implanted into a womb. Therefore, I do not believe it should be called an embryo or that it is in fact human life.

At about 3 to 5 days, a blastocyst is formed which contains an inner cell mass comprised of a very small number of non-programmed cells, something so small it cannot be seen by the naked eye. The research value of these cells, however, is enormous. They have the potential to form any cell in the body and can reproduce indefinitely. Studies in animals demonstrate that this could lead to cures and treatment for millions of Americans.

As exciting as that is, it is only part of the story. When combined with stem cell research, SCNT could be used to develop new and innovative treatments that allow cells, tissues, and organs to function again.

Let me explain. When cells, including donated organs, tissue, or blood, are transplanted or transfused, the recipient's body mounts a rejection response, attacking these cells as foreign. However, if a patient's own somatic cells were the source of stem cells used to create therapeutic cells or tissues, immunological rejection could be avoided since the cells and the tissues would exactly match those of the person who donated the somatic cell nucleus. Therefore, SCNT could allow a patient's own cells to be used to treat or cure that patient's disease.

Although some believe that stem cell research could proceed without SCNT, the overwhelming majority of scientists believe that SCNT is essential to turn the research into cures and treatments that actually help patients. For example, both the National Institutes of Health and the National Academy of Sciences have recently released reports that stress the importance of this specific type of research. Scientists are joined by a wide range of patient advocacy groups for which this research is a matter of life and death.

Unfortunately, this is precisely the research that would be banned by H.R. 2505 that passed the House and the pending proposal sponsored by Senator Sam Brownback. Senator Brownback is a good friend and I certainly do not question his motivation for sponsoring this legislation. As one who is also pro-life, I too have struggled with this issue. I am concerned, however, about the impact this bill will have on the future of the biomedical research.

In addition to shutting the door on important research, these bills will limit patient access to potentially life-saving products. And according to the legislation, if a drug or treatment for a disease is developed overseas in a country that allows the use of cloning for research purposes, it will not be available to patients in the United States, even if the FDA finds that it is safe and effective. Thus, Americans would be denied access in this country to cures and treatments, while citizens of other nations receive the benefits of these products.

Fear and misunderstanding about biomedical research is not new. In the mid-1970's, for example, recombinant DNA research was at a similar crossroad. We can all recall the fear by some that mad scientists were going to create a Frankenstein monster. Some in Congress called for banning recombinant DNA research. And they were wrong.

Fortunately, Congress did not ban the research. The research continued and millions patients and their families have benefitted. Today, recombinant DNA research is used to produce human therapeutics to treat a wide variety of diseases and conditions. These products include human insulin for diabetes, Herceptin for breast cancer, Epogin for patients with kidney disease, Pulmozyme that has prevented death in children with cystic fibrosis, and Cerezyme for Gaucher's disease.

Yet, nearly 30 years later, the Senate is poised to debate legislation that could permanently shut off a different but equally important and promising area of biomedical research. This simply must not happen.

The United States has long been the world's leader in medical research. This research has benefitted our citizens who have access to the best medical care and newest treatments. It has also been good for our economy, as it has created hundreds of thousands of high-paying jobs.

Tougher restrictions targeted at reproductive cloning are necessary, but shutting down SCNT, even for a short time, runs counter to our history and tradition. More importantly, it will deny Americans access to the best medical treatments.

Senator Specter, as you know, I have lived the terrible ordeal of watching a loved one confront a disease without a cure. Therapeutic cloning, SCNT, is controversial, but it raises new hopes that must be explored. And I urge the Senate not to deny hope to millions of families coping with deadly diseases by criminalizing this vital research.

Thank you, Senator Specter.

[The statement follows:]

PREPARED STATEMENT OF FORMER SENATOR CONNIE MACK

Mr. Chairman, Senator Specter, and Members of the Subcommittee, it is a pleasure to appear before this subcommittee, on which I had the great honor of serving.

Before I begin my testimony on the subject of today's hearing, let me commend and thank the Members of this subcommittee for your bipartisan effort to achieve the goal to double funding for the National Institutes of Health. With your continued leadership, this historic effort will be completed in fiscal year 2003. I am convinced that we will continue to see significant advances in science and medicine for many generations to come as a direct result of the basic and clinical research that has been conducted during this five-year period.

This marks the first time since I retired from the United States Senate that I have testified before my former colleagues. But I feel so strongly about the possibility that the Congress of the United States might actually criminalize important biomedical research that I have to speak out. As you may be aware, one of my main areas of interest, and where my passion truly lies, is biomedical research. Today, I am involved with several biomedical research entities, precisely so I can help make a difference in advancing this important effort.

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This research is sometimes referred to as cloning. But all cloning is not the same. One type which most believe should be stopped is the cloning of humans. It is called reproductive cloning. But there is another type, called therapeutic cloning, which could be used to replace damaged cells and tissues. SCNT research is an example of therapeutic cloning, and it is this type of research that some want to criminalize.

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It is important to make the clear distinction between reproductive and therapeutic cloning. For therapeutic purposes, scientists use a technique they call somatic cell nuclear transfer or "SCNT".

Here's how it works: First, the nucleus of an egg cell is removed. In its place, researchers insert the nucleus of an already differentiated cell (a cell that performs a specific function in the body). Chemicals are added to stimulate the egg to start dividing. This egg cell is never fertilized by sperm, and will never be implanted into a womb. Therefore, I do not believe should be called an embryo, or that it is human life.

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Let me explain: When cells, including donated organs, tissues or blood, are transplanted or transfused, the recipient's body mounts a rejection response, attacking these cells as foreign. However, if a patient's own somatic cells were the source of stem cells used to create therapeutic cells or tissues, immunological rejection could be avoided since the cells and tissues would exactly match those of the person who donated the somatic cell nucleus. Therefore, SCNT could allow a patient's own cells to be used to treat or cure that patient's disease.

Although some believe stem cell research could proceed without SCNT, the overwhelming majority of scientists believe SCNT is essential to turn that research into cures and treatments that actually help patients. For example, both the National Institutes of Health and the National Academy of Sciences have recently released reports that stress the importance of this specific type of research. Scientists are joined by a wide range of patients advocacy groups, for whom this research is a matter of life and death.

Unfortunately, this is precisely the research that would be banned by H.R. 2505 that passed the House and the pending proposal sponsored by Senator Brownback. Senator Brownback is a friend, and I certainly do not question his motivation for sponsoring this legislation. As one who is also pro-life I, too, have struggled with this issue. I am concerned, however, about the impact this bill will have on the future of biomedical research.

In addition to shutting the door on important research, those bills will limit patient access to potentially life-saving products. According to the legislation, if a drug or treatment for a disease is developed overseas in a country that allows use of cloning for research purposes, it will not be available to patients in the United States—even if the FDA finds that it is safe and effective. Thus, Americans would be denied access in this country to cures and treatments, while citizens of other nations receive the benefits of these products.

Fear and misunderstanding about biomedical research is not new. In the mid-1970's, for example, recombinant DNA research was at a similar crossroad. We can all recall the fear by some that mad scientists were going to create a Frankenstein's monster. Some in Congress called for banning recombinant DNA research. They were wrong.

Fortunately, Congress did not ban that research. The research continued, and millions of patients and their families have benefited. Today, recombinant DNA research is used to produce human therapeutics to treat a wide variety of disease and conditions. These products include human insulin for diabetes; Cerezyme for Gaucher disease, Herceptin for breast cancer; Epogin for patients with kidney disease and Pulmozyme that has prevented deaths in children with cystic fibrosis.

Yet, nearly 30 years later, the Senate is poised to debate legislation that could permanently shut off a different, but equally promising, area of biomedical research. This simply must not happen.

The United States has long been the world's leader in medical research. This research has benefited our citizens who have access to the best medical care and newest treatments. It has also been good for our economy, as it has created hundreds of thousands of high-paying jobs.

Tougher restrictions targeted at reproductive cloning are necessary. But shutting down SCNT—even for a short time—runs counter to our history and tradition. More importantly, it will deny Americans access to the best medical treatments.

I've lived the terrible ordeal of watching a loved one confront a disease without a cure. Therapeutic cloning, SCNT, is controversial, but it raises new hopes that must be explored. I urge the Senate not to deny hope to millions of families coping with deadly diseases by criminalizing this vital research.

Senator SPECTER. Thank you very much, Senator Mack, for that testimony. Senator Harkin asked me, in taking the assignment to Chair this hearing, to give you his special personal thanks because we know you have come from Florida, and he wanted to express his special appreciation to you.

Senator MACK. Thank you.

Senator SPECTER. We now turn to Congressman Bart Stupak, elected to the House of Representatives in 1993, and before that he served in the Michigan State House of Representatives and has a background in the law, receiving his law degree from Thomas Cooley Law School, after his bachelor's degree from Saginaw Valley State College. And he also has had a career in law enforcement as a State trooper with the Michigan Department of State Police.

Congressman Stupak joins us today to present the other view because the subcommittee is committed to hearing both sides and giving all sides an opportunity to be heard.

Congressman Stupak, thank you for joining us, and we look forward to your testimony.

STATEMENT OF HON. BART STUPAK, U.S. REPRESENTATIVE FROM MICHIGAN

Mr. STUPAK. Thank you, Mr. Chairman, and thank you for holding this hearing.

I am here today to speak in strong support of Senate bill 1899, Senator Brownback's counterpart to H.R. 2505, the Weldon-Stupak Human Cloning Prohibition Act of 2001.

On July 31, the House approved our legislation banning the cloning of human embryos. It passed the House by a vote of 265 to 162. 265 Members of the House voted to ban the cloning of human embryos. 265. This is not a number that can be explained by arguments such as "all the pro-lifers voted for it" or "those who oppose embryonic stem cell research voted for it." Many more voted for it after they looked at other legislation.

We are in the midst of a tremendous new debate, of a new policy direction during a medical revolution. We cannot afford to treat the issue of human embryo cloning lightly whether for research or reproduction, nor can we treat it without serious debate and deliberation.

The need for action is clear. Researchers have publicly announced their intention to begin human cloning for profit. Research firms have cloned human embryos for research purposes here in the United States and in China. Whatever your belief is about embryonic stem cell research, the fact is embryos are biologically human entities.

We must ask ourselves what is the message we wish to send on behalf of the American people?

Before we decide what this message is, we must answer these questions. What makes up human beings? What is the human spirit? What moves us? What separates us from animals? These questions are the center of this debate.

What will the message of the U.S. Congress be? Will it be a cynical signal that human embryo cloning and destruction is okay, acceptable, even to be encouraged, all in the name of science? Or will our message be one of urging caution and care? If we allow this research to go forward unchecked, what will be next? Unchecked research. Does it mean that once embryo cloning is considered safe, we will then allow parents to choose what color hair or eyes their baby will have? Would we allow scientists to manufacture children with greater intelligence in the pursuit of the perfect human being?

We need to consider all aspects of cloning and not just what researchers tell us is beneficial.

Opposition to our legislation has based their objections on arguments that it will stifle research, discourage free thinking, and put science back in the dark ages. This is simply ridiculous. Our bill does nothing of the sort. It allows animal cloning. It allows tissue cloning. It allows current stem cell research done on existing, normal embryos. It allows DNA cloning. How is this stifling medical or scientific research?

These scientists who are pushing so hard to be allowed a free pass for research on what constitutes the very essence of what it is to be a human do not know what goes wrong with cloned animal embryos. The horror stories are too many to mention here, deformed mice and deformed sheep developing from cloned embryos.

A prominent researcher working for the bioresearch companies has admitted scientists do not know how or what happens in cloned embryos resulting in these deformities. In fact, he calls the procedure when the egg reprograms DNA magic.

Magic. This is hardly a comforting, hard-hitting scientific term, but it is accurate. It is magic.

Opponents of our bill have said therapeutic cloning is the Holy Grail of science which holds the key to untold medical wonders. To our opponents, I would say show us these miracles. Show me the wondrous advances done on animal embryonic cloning. But these opponents cannot demonstrate these advances because they do not exist.

Our ability to delve into the mystery of life grows exponentially. All fields of science fuse together to enhance our ability to go where we have never gone before. The question is this: simply because we can do something, does that mean we should?

What is the better path to take? One in which we mass produce cloned embryos in the lab, a path which will lead to producing cloned babies? Or is the better path one urging caution, stepping

forward based on sound science guided by ethical, moral, and legal principles?

The human race is not open for experimentation and manufacture at any level, even at the embryonic level, is uncalled for. Has the 20th century not shown us the folly of this thought?

Holy Grail? Magic? How about the human soul? Scientists and medical researchers cannot find it, and most importantly, they cannot medically explain it. Still, writers write about it. Songwriters sing of it. You and I believe in it. From the depth of our souls, we know that we should ban human cloning.

Mr. Chairman, thank you for the opportunity to be here. If you have any questions, I will be happy to try to answer them.

[The statement follows:]

PREPARED STATEMENT OF CONGRESSMAN BART STUPAK

Mr. Chairman and distinguished members of this panel, I am here to speak in strong support of S. 1899, Senator Brownback's counterpart to H.R. 2505, the Weldon-Stupak Human Cloning Prohibition Act of 2001.

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What makes up human beings? What is the human spirit? What moves us? What separates us from animals?

These questions are the center of the debate.

What message will the United States Congress send? Will it be a cynical signal that human embryo cloning and destruction is okay, acceptable, even to be encouraged, all in the name of science? Or will it be a message urging caution and care? If we allow this research to go forward unchecked, what will be next? Unchecked research, does it mean that once human cloning is considered safe, we will then allow parents to choose what color hair and eyes their baby will have? Would we allow scientists to manufacture children with greater intelligence in the pursuit of perfected humanity?

We need to consider all aspects of cloning, and not just what researchers tell us is beneficial.

Opposition to the Brownback-Weldon-Stupak bill has based their objections on arguments that it will stifle research, discourage free thinking and put science back in the dark ages. How ridiculous. Our bill does nothing of the sort. It allows animal cloning; it allows tissue cloning; it allows current stem cell research done on existing normal embryos; it allows DNA cloning. How is this stifling research?

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Our ability to delve into the mysteries of life grows exponentially. All fields of science fuse together to enhance our ability to go where we have never gone before.

The question is this: simply because we CAN do something, does that mean we SHOULD?

Which is the better path to take? One in which we mass produce cloned embryos in the lab, a path which will lead to producing cloned babies? Or is the better path one urging caution, stepping forward based on sound science guided by ethical, moral, and legal principles?

The human race is not open for experimentation and manufacture at any level, even the embryonic level. Hasn't 20th-century history shown us the folly of this?

Holy Grail? Magic? How about the human soul? Scientists and medical researchers can't find it, and most importantly they can't medically explain it. Still writers write about it; songwriters sing of it; you and I believe in it. From the depths of our souls we know we should ban human cloning.

Thank you.

Senator SPECTER. Thank you very much, Congressman Stupak. I do have a few questions.

Senator Mack, you have put your finger right on the issue in two sentences of your prepared statement. "The egg cell is never fertilized by sperm and will never be implanted into a womb. Therefore, I do not believe it should be called an embryo or that it is in fact human life." Would you amplify on your view, what you summarized there?

Senator MACK. I sure will. Those two sentences were not there by mistake. It is something I have given a great deal of thought about. As I indicated in my prepared testimony, I consider myself to be pro-life, and so the question I had to ask is, if I am pro-life, how do I address this important issue? It seems to me the very first question you have to ask yourself, is this in fact human life that we are dealing with? Two points.

One, I made the comment with respect to it should not be called an embryo because I want to challenge the scientific community to begin to define in essence new entities that have not existed before in biology. The world has changed dramatically. We cannot be using terms that were created 30, 40, 100, 200 years ago to be used in the debate about this new technology.

The question I had to ask myself was, again, when does life begin? I believe life begins at conception. Then the question becomes, what is the definition of conception?

I suppose that most who accepted that notion that life begins at conception accepted that notion without there ever being a thought passing through their minds that at some point in the future there would be the ability to take the nucleus out of a somatic cell and transfer it into an egg.

Therefore, again, the purpose there is to challenge, is to say that we need to be defining words that properly express what is taking place today. And I just do not believe that an egg, where the nucleus of the egg has been removed, and the somatic cell nucleus has been replaced in it, is human life. So, that is where I begin the discussion and I make decisions from there with respect to whether this should be the type of research we should pursue.

Senator SPECTER. Well, when we get into the question of when life begins, we are in very deep philosophical areas.

Congressman Stupak, in your statement, you say that your bill allows animal cloning, it allows tissue cloning, it allows current

stem cell research done on existing normal embryos, it allows DNA cloning, what do you mean when you say that your bill allows tissue cloning?

Mr. STUPAK. Well, Mr. Chairman, as you know, any excess embryos right now are used for research. Tissue cloning can also be developed through the bill that we currently have before you.

If I can summarize it, our whole objection to this is we do not want—and we are drawing an ethical line here, maybe a legal, and maybe even moral at the special creation of embryos for research purposes. We need to respond to that cloning research precisely because it involves the special creation of cloned embryos for the sole purpose—for the sole purpose—of research. So, you can do research right now. There are guidelines. NIH and others are allowed to do it right now with the excess. What we are saying, we do not want human embryo farms, if you will, for the sole purpose of research. We think that would be inappropriate.

Senator SPECTER. Are you saying that you would be willing to see existing embryos, existing eggs used with the DNA removed and DNA from, say, a Parkinson's patient, as long as there are not embryos created artificially?

Senator MACK. Not created artificially. And again, you have the adult stem cell research that is being done that shows great promise. We think the current policy—again, even if you take a look at President Clinton's Bioethics Commission, they also fully recognize that any efforts in humans to transfer a somatic cell nucleus into an enucleated egg involves the creation of an embryo. And they said that is where we draw the line. As long as you do not pass that line. Those are the standards currently in the Bioethics Commission. So, that is where we are drawing the line, Senator.

Senator SPECTER. So, you have an objection even if the process does not scientifically create an embryo. You had said in your testimony that you do not want to see embryos created.

Mr. STUPAK. He says as long as you are not going to create an embryo that is not going to be planted in a woman's womb. If you can create human embryos that can produce human when brought to full term, how are you ever going to stop the private doctor from implanting that into a womb in the privacy of his office?

Senator SPECTER. Well, you pass a law which prohibits it and you attach penalties to it. You have the same issue with the Weldon-Stupak bill. You are not going to stop somebody from doing it if they choose to violate the law, run the risk of being apprehended and punished.

Mr. STUPAK. See, what we are saying in the Weldon-Stupak-Brownback bill is do not even start down that, do not start using human cloning because once you do this, the next step is to plant it in the womb for your human cloning. How do you stop it then? Why even open the door to it until we know where we are going with this whole situation in medical research?

Senator SPECTER. I understand the slippery slope argument, but the effect of a prohibition would be the same in your bill if you say you cannot have human cloning. There is a consensus not to have human cloning.

When you come to grips with the core as to what Senator Mack has said, the egg cell is never fertilized by sperm and will never

be implanted in a womb. Do you disagree with the assertion that there is a risk that it will be implanted in a womb?

Mr. STUPAK. Yes.

Senator SPECTER. Well, how is your bill any more effective in stopping implanting in a womb than the Harkin-Specter bill which prohibits implanting it in a womb?

Mr. STUPAK. Our bill says, look, we need to respond at research cloning. We do not want research cloning farms, if you will. You have ACT up in Massachusetts. You have China. You have others who are saying we are going to mass produce human cloning. We will pick and choose what we want. We discard the rest. That is what we do not want to see happening, and that is where I think our bill differs from the other bills out there. On the House side, it was the Greenwood bill.

Senator SPECTER. I think Congressman Greenwood and others and I would be willing to ban the so-called embryo farms and ban human cloning.

Let me ask you this question. Recently there have been comments about being able to help someone who has Alzheimer's in their background. You have raised the issue about where you go on unchecked research creating the option of hair color and eyes, which I grant you is along a, perhaps, frivolous line. But what if you have an Alzheimer's gene and scientists have the capability to help an individual who has that Alzheimer's gene and had it in the family for generations? What if you have an opportunity, when that individual is having a child, to alter that gene to preclude Alzheimer's would you disagree with that?

Mr. STUPAK. Well, we think our bill, because it does allow embryo stem cell research, that your hope for Parkinson's, from what medical science tells us, probably lies best right there. We do not prevent embryo stem cell research. Even the opponents of the bill admitted during the debate on July 31 on the floor that our bill to ban embryonic stem cell research is not before us. That was not the issue before us. We still allow medical science to go forward, whether it is animal cloning, tissue cloning, stem cell research, DNA cloning. We allow that. What we are saying is do not create life and then disregard what you do not want. That is what we are in fear of.

I know you said abandon the farm. It is more than just abandoning the farm. Are we really abandoning some basic ethical, moral, and legal principles? This is a debate we should have as a country. And I am glad to see the Senate and the House has had that debate.

And that is why those who voted for our ban in the House were not just pro-lifers or those against stem cell research or other research. They looked at the merits of the total bill, and when they looked at it, they said, as the Bio Commission under President Clinton said, there is a legal, ethical, and moral line we should not cross. And our bill allows the research without crossing that line.

So, I am pleased to be here today to join you in this debate.

Senator SPECTER. Well, come back to my question. I have not gone into the stem cells. Frankly, I would like to, but we have another panel of witnesses. But come back to the question I am asking you, which is a very narrow question.

I will agree with you that we should not alter genes for the color of eyes or hair, but should we alter the gene if you can preclude the next generation from having Alzheimer's?

Mr. STUPAK. No, you should not. But what we are saying is do not create life and then take the gene you want and then abandon that life.

Senator SPECTER. Well, you would not be abandoning the life. You would simply have the embryo with a modification to take away the gene that would otherwise cause the individual to have Alzheimer's.

Mr. STUPAK. And that embryo, if you will, would grow on to life if you allowed it to naturally develop. Correct?

Senator SPECTER. Correct.

Mr. STUPAK. So, you are going to start modifying life in order to a cure somewhere else. That is where we have the problem.

Senator SPECTER. You disagree with modifying the gene to stop that individual-to-be from having Alzheimer's.

Mr. STUPAK. Oh, I thought you said modify the embryo to take a benefit to give to another embryo.

Senator SPECTER. Well, scientists have a way, they say, now to alter the gene which causes Alzheimer's. And my question to you is, would you agree that it would at least be worthwhile to allow scientists to do that?

Mr. STUPAK. And I believe with the DNA cloning, that is allowed in our legislation. You could accomplish that, yes. We allow that DNA cloning in our bill. We do not prevent it.

Senator MACK. Mr. Chairman, if I may make a couple additional comments.

Senator SPECTER. I was just about to ask you to do that, Senator Mack.

Senator MACK. With respect to the term "farming," it does bring up all kinds of pictures, I am sure, in everybody's mind that here is that phraseology. I am sure that if you go back and listen to the debates, for example, about human organ transplants, the terms that were used like "harvesting" and "farms," and this was a terrible thing we were moving into. The reality is that because someone who supports my position that somehow or another as lost their moral sense or their ethical track and would not put in place things to keep markets from developing and farms from being created is a real stretch from my perspective.

I guess an additional point that I would like to make is that there is the impression that when a new technology comes along, that there is no ability to control it. It has either got to be used all for good or all for evil. But I would make the point that the core of all human progress is rooted in our ability to manage the harmful consequences of innovation. That has been the history of humanity.

You could make the same argument about fire. I am sure that sitting around in darkness years ago, there were some real warnings about what could happen if this new technology, fire, got into the wrong hands. And sure enough, there are dangers, but that does not mean we should eliminate that progress that can come from that new technology. I think that our society has indicated

over and over and over again the ability to control the environment around these new innovations that we develop.

Senator SPECTER. Congressman Stupak, you mentioned your bill does not limit stem cell research, and as we all know, the President allows Federal funding to be used on stem cells in existence as of August 9 at 9 p.m. when he made his speech. Do you believe that that limitation is sound, just to cut off Federal funding on stem cell research as of that date and that time because that was the time of the President's speech?

Mr. STUPAK. Well, I think the President at that time and that date, based upon the best information available to him, made that decision. But I also believe the President said he would leave the door open for further review. And if there is sound medical purpose to go forward, he would review it at a later date. But based upon the information, the strands known at that time, that is what he thought was the most prudent action. And I support him in that position. But I did not think he forever closed the door. I thought he left it open for further research.

Senator SPECTER. So, you would say that if those stem cell lines are inadequate for research, that you would consider using stem cell lines developed at a later time.

Mr. STUPAK. Yes, I would. Again, our bill does not prohibit. We do not put number of lines in there as of 9 p.m. on a certain evening. We just said you still can do your stem cell research in our legislation.

Senator SPECTER. Senator Mack, what would you say—and I intend to quote you on the Senate floor—would be the kernel and the strongest argument to tell our pro-life colleagues in the Senate. And Senator Thurmond testified at that table and in that chair in the same way.

Senator MACK. In the same way? I am just kidding.

Senator SPECTER. Not in an identical way.

Senator MACK. Not in a cloned way. Is that what you are trying to say?

Senator SPECTER. That is right.

Not identical twins. But if any of us does as well at 99½ as Strom is doing today, it would be a great tribute to all of us.

But I reference Senator Thurmond's testimony, because he is in favor of nuclear transplantation.

But to sum up. What would the argument be, since you will not be on the Senate floor to advance it, to tell your ex-colleagues, who have a great deal of respect for you, why a strong pro-life Senator like Connie Mack favors nuclear transplants and stem cell research?

Senator MACK. I think I would start by asking them to consider the base of knowledge that we have today compared to what knowledge we had 15, 20, 30 years ago. And the point that I am making there is that as new knowledge is developed, it gives you a new way to look at issues that are challenging you. Not that you change your perspective with respect to your values, but the new knowledge creates a new environment in which to take a look at the question of whether we should allow somatic cell nuclear transfer.

And that is why I raised the question in my testimony about the whole issue of life. Bart has indicated, and I think quite accurately,

that if it is human life, it has to have special treatment. But there are those of us who believe that there is something fundamentally different between an egg that is fertilized by a sperm and in the womb versus an egg that has received a somatic cell nuclear transfer and will never be placed in a womb and will never be able to develop.

I believe I am correct in this, that the blastocyst, which is a phase that the cells go through in development, does not normally attach to the womb until after the blastocyst stage. The point is, from my perspective, again it is not human life if it has not been fertilized by sperm. It is not human life if it has not been placed in the womb.

I go right to the heart of the issue. I suspect that there would be people who could conclude that it is some form of human life. Then the question becomes, well, what kind of legal protections does that some kind of human life receive? And I think the question then becomes one of, well, what are the potential benefits by continuing the research even under those circumstances.

So, I think there is a series of places that Members are going to find themselves in this debate, but to me you have to start fundamentally with asking the question when does life begin, is this life, and then move from that point on.

Senator SPECTER. So, your essential point is that it is not conception and therefore not life.

Mr. STUPAK. If I may just—

Senator SPECTER. Congressman Stupak, I was going to ask you if you had any concluding comments.

Mr. STUPAK. Sure. I think maybe there is a little difference between myself and my friend, Connie Mack here.

I asked that question at the hearing. I sit on the Energy and Commerce Committee, the Health Subcommittee. And when the experts came to testify, the commission, the National Biological Advisory Commission, President Clinton's Bioethics Commission, Mr. Tom Okamura, I asked the question. I said, the blastocyst. Is that not really another term for an early living human embryo? The answer was, yes it is, absolutely.

And we do not mean to obfuscate the intent or the actuality about what we are talking about here. So, what we are saying, even a blastocyst that my friend talks about—if the expert tells us it is a living human embryo, how can you manipulate, modify it for the benefit of another?

Senator SPECTER. Okay. Thank you very much, Senator Mack, Congressman Stupak. We very much appreciate your being here.

We now turn to our next panel: Dr. Gerald Fischbach, Mr. Silviu Itescu, and Mr. Kevin Kline.

Dr. Fischbach is vice president for Health and Biomedical Sciences, Dean of the Faculty at the School of Medicine at Columbia. He was the Director of the National Institute of Health for Neurological Disorders and Stroke. Prior to his appointment as Director, Dr. Fischbach served as director of the Neurobiology Departments of the Harvard Medical School and the Massachusetts General Hospital. His M.D. is from Cornell University Medical School.

Welcome, Dr. Fischbach. You have been very generous with your time to this subcommittee on a number of occasions, and we thank you for coming again today and look forward to your testimony.

STATEMENT OF GERALD D. FISCHBACH, M.D., EXECUTIVE VICE PRESIDENT FOR HEALTH AND BIOMEDICAL SCIENCES, DEAN OF THE FACULTY OF MEDICINE, COLUMBIA UNIVERSITY

Dr. FISCHBACH. Thank you, Senator Specter. I want to thank you for inviting me back to comment on the important subject of this committee's hearing.

This committee, led by you and Senator Harkin, has inspired this Nation's scientists and given great hope to millions of patients in this country by your work here in furthering research in this country.

I am the vice president for Health and Biomedical Sciences at Columbia. I am here today representing the Coalition for the Advancement of Medical Research which represents 60 universities, scientific societies, and patient advocacy groups.

I want to do a few things in the next 4 minutes. First, I want to reiterate my support for human embryonic stem cell research. There is no question that this research has enormous promise in a new type of restorative or regenerative medicine in which we will be able to treat devastating, degenerative disorders not merely by treating their symptoms, but by stopping the course of the disease and perhaps even reversing some of the processes underlying the disease. And by that, I mean the ones we have talked about in the past involving the nervous system and also degeneration of cells in the pancreas that lead to diabetes and degeneration of cells in the heart and other tissues of the body.

There have been a number of successes in the past 3 or 4 years after the initial discovery of human embryonic stem cells. Stem cells have been used in animal models to reverse the course of Parkinson's disease. They have been used to repair spinal cord injury. They have been used to minimize the damage in stroke. They have been used to reverse almost all of the symptoms of diabetes in animal models.

The second point I want to emphasize is that somatic cell nuclear transfer would greatly facilitate research on embryonic stem cells. It would increase the supply of cells and it would answer in large part, if not entirely, one of the main remaining problems, that is, the rejection of cells once they are implanted and after they have initially been shown to be successful.

One of the great tragedies of this type of research would be the reversal of fortune after an initial success. Somatic cell nuclear transfer, for technical reasons I would be glad to discuss later, offers the possibility of minimizing rejection of stem cells once implanted.

Third, I want to make clear that I do not support attempts at human cloning. I distinguish human cloning from somatic cell nuclear transfer, and I know of no responsible scientist who is in favor of nuclear cloning at this point. There are too many unknowns. It is inconceivable that we would produce another Arlen Specter or another Kevin Kline. There are instantaneous, every-instant interactions with our environment and modifications of our genetic makeup that distinguish one individual from another. So,

the possibility of human cloning is beyond our scientific reach and imagination today.

Finally, I want to comment on one aspect of the Landrieu-Brownback bill which criminalizes work on stem cells derived from young embryos created by somatic cell nuclear transfer. These criminal penalties would be placed on scientists and on patients that seek treatments developed in other countries such as Great Britain where SCNT is currently legal. Under this bill, Americans who travel to another nation to benefit from the medical technology, denied to them in the United States, would be considered criminal. If a cure or a treatment were developed in another country using nuclear transplantation, Americans would be alone in the world in being unable to take advantage of such treatment.

Largely as a result of this committee's leadership, American biomedical science has flourished these past several years. Increased funding, I believe, has been managed extraordinarily well by Federal agencies, and real advances have been made in many areas crucial to the physical and mental health of this country.

I believe that criminalizing this type of work will cast a pall over the country's scientific effort. Individuals are not undertaking research for research's sake. Most of them are undertaking research to help improve the health of this Nation, and I think the criminal implications would have aspects that reach far beyond somatic cell transfer.

We all have ethical obligations. We have talked about the very profoundly troubling ethics of the derivation of stem cells, but we all have ethical obligations to our parents, our children, and our colleagues who suffer from debilitating disorders. We must do all we can to alleviate them. We cannot approach such critical matters with one hand tied behind our backs. We must be able to pursue this promising, extremely promising, area of medical research with the full force of our intellect and abilities.

I believe if this bill passes, it will stand in the way of the ability of scientists and physicians to treat their patients with the best tools available.

[The statement follows:]

PREPARED STATEMENT OF DR. GERALD D. FISCHBACH

Mr. Chairman, Senator Specter, members of the Committee, thank you for inviting me here today to testify before you about this most important topic. I am pleased to join the other respected witnesses this morning. For the Record, my name is Gerald D. Fischbach, Executive Vice President for Health and Biomedical Sciences at Columbia University. I also serve as Dean of the Faculty of Medicine at the Columbia University College of Physicians and Surgeons.

I am here today representing the Coalition for the Advancement of Medical Research (CAMR). The coalition is comprised of more than 60 universities, scientific societies, patients' organizations, and other entities.

There are three major points I would like to discuss this afternoon: reproductive cloning, nuclear transplantation, and the denial of medical treatments developed in other countries to Americans.

To begin, I want to make it as clear as possible that no responsible scientist that I know of supports efforts to clone a human being. As stated in the recent National Academies of Science report on the topic, "it is dangerous and likely to fail." In testimony on this issue before other Senate Committees, my esteemed colleagues Paul Berg and Irv Weissman have made that point clear and I echo their remarks. This is something upon which we can all agree.

The second point I would like to make revolves around the portion of the Landrieu/Brownback bill that criminalizes a scientific procedure known as nuclear

transplantation. I should begin by pointing out that, despite what one might see in science fiction and horror movies, not all cloning is bad. In science, the term "cloning" describes the preparation of an infinite number of copies of a single molecule, virus, or bacterium.

DNA cloning has been used to map out the human genome sequence. It has been used to uncover genes that cause human diseases such as Alzheimer's disease, heart disease and many forms of cancer. It is used to identify the nature and origin of dangerous bacteria in the fight against bioterrorism. DNA typing is used in many modern forensic procedures, allowing the innocent to be freed and the guilty to be convicted.

Cloning has also been used in the production of many important drugs such as human insulin. The cloning of cancer cells from cancer patients is a procedure that has been done for years in an effort to identify promising cancer therapies.

S. 1899 would deny Americans access to treatments for some of the most debilitating diseases known to medicine. Without being able to match new treatments with an individual's own DNA, our ability to cure and treat disease may well be greatly hindered. It would also bring about a serious chill on scientific research in the United States. If this procedure is deemed to be unacceptable by some and therefore made illegal, what assurance does the next generation of scientists have that their particular field of cutting edge investigations might not also suffer the same fate? Given that uncertainty, who among us would take the risk of pursuing a career in science? We are at a point in history when we need young researchers to forge new scientific frontiers in an effort to fight bioterrorism and battle disease. Labeling them as criminals undermines these efforts and does no good.

Finally, Mr. Chairman, the third point I would like to discuss is the importation portion of the S. 1899 that has, for some unknown reason, gained little or no attention. This section of the bill enacts criminal penalties against doctors and patients who seek to access treatments developed in other countries using nuclear transplantation. Under this bill, physicians could not treat their sick patients with an effective treatment developed overseas using nuclear transplantation. Similarly, an American who travels to another nation to take advantage of a medical technology unavailable in the United States could be considered a criminal. If a cure or treatment for Parkinson's disease or Alzheimer's disease were developed in another country using nuclear transplantation, Americans could be alone in being unable to take advantage of that treatment. I cannot believe that the United States Senate would pass such legislation.

Doctors, like Senator Frist and I, have an ethical obligation to our patients to do all we can for them. This bill, if passed, sharply curtails the ability of doctors to properly treat their patients.

Those in support of this legislation argue that these drastic measures are necessary to prevent a slide down the slippery slope of medical horrors that we all deem unacceptable. I disagree with that line of reasoning. Despite the wild claims that some supporters of S. 1899 have made in their ads, we can prevent reproductive cloning without interfering with science. The bill that the Chairman and Ranking Member have sponsored, S. 1893, does just that, as does Senator Feinstein's bill.

I implore you, ban reproductive cloning, but do not make somatic cell nuclear transfer (therapeutic cloning) illegal. SCNT holds the potential to help scientists find cures for such debilitating diseases as ALS, Parkinson's, Juvenile Diabetes, and others. Chairman Harkin and Senator Specter, largely as a result of your leadership, support for biomedical research in this country has risen tremendously in recent years. It would be a sad and strange irony that, if at the same time the resources we have at our disposal are increasing, this Congress were to take away such a powerful and important research tool. Thank you.

Senator SPECTER. Thank you very much, Dr. Fischbach.

We now turn to Dr. Itescu, director of Transplantation Immunology, Columbia Presbyterian Medical Center, New York-Presbyterian Hospital. He is a member of the American Board of Internal Medicine and a consultant for global clinical affairs of CSL Limited. He received a bachelor of medicine and bachelor of surgery from Monash University School of Medicine, Melbourne, Australia.

Thank you for joining us, and we look forward to your testimony.

**STATEMENT OF SILVIU ITESCU, M.D., DIRECTOR, TRANSPLANTATION
IMMUNOLOGY, NEW YORK-PRESBYTERIAN HOSPITAL, COLUMBIA
UNIVERSITY, NY**

Dr. ITESCU. Thank you very much. I would like to thank the committee for inviting me here to speak really on some alternative type of stem cells and where I think some aspects of research are going and some areas where I think we should progress perhaps more slowly rather than jump in.

I am director of Transplantation Immunology at New York-Presbyterian Hospital of Columbia University, and my field is to provide specialist input into the use and management of immunosuppressive drugs for patients with various solid organ transplants, most notably the heart.

Congestive heart failure remains a major public health problem. In western societies, it is primarily the consequence of a previous heart attack. Current therapy of heart failure is limited to the treatment of already established disease and is really pretty insufficient. For patients with end-stage heart failure, the current treatment options are extremely limited, and less than 3,000 patients are offered heart transplants annually due to the severely limited supply of donor organs. So, clearly, development of approaches that prevent heart failure would be preferable to those that simply ameliorate established disease.

My research group has recently identified a specific population of stem cells in human adult bone marrow which can be delivered to the heart after a heart attack and enables the development of many tiny blood vessels. In a well-characterized animal model, this results in protection of heart muscle cells against death through starvation and results in long-term improvement of heart function. We have recently received NIH approval to support funding of further research using these adult stem cells, and are in the process of obtaining our institutional IRB approval to begin safety studies of this therapy.

The notion that adult tissues contain stem cells, other than those needed to reconstitute bone marrow elements, is relatively new, particularly with respect to regeneration of tissues that are not normally renewed, such as heart, neuronal, or muscle. In recent years, several investigators have shown that neural stem cells, as well as hematopoietic and other types of stem cells, can be identified and obtained from adult tissues and that such cells can give rise to different tissues such as liver, brain, blood, or muscle, suggesting really the presence of one or more types of typical pluripotent stem cells in adults.

While the full developmental options of such adult stem cells are not fully known, it has become evident that when you put such cells into one area, they can transform into a different type of cell, and that is called transdifferentiation. More recently, adult bone marrow-derived cells, when injected into the spinal cord of rats, for example, with spinal cord transection, transdifferentiated to become myelin-producing cells. There are many examples of such situations where differentiation to neurons and other tissues has been shown. Such investigators have suggested that bone marrow cells could, in principle, be harvested from a patient and used for a po-

tential cell therapy for diseases such as neurodegenerative diseases.

What all of these recent studies have in common is to emphasize the potential for use of adult tissue as an alternative to embryonic tissue. If in fact adult tissues contain multipotent stem cells capable of sufficient self-renewal and differentiating capability, this would provide a far more elegant and preferred approach since autologous cells will not induce any immunological reaction and no immunosuppression will be needed. In contrast, embryonic stem cells will always be seen as foreign by the recipient and some degree of immunosuppression is likely to be required.

While adult bone marrow stem cells appear to have the ability to replicate to greater levels than other adult cells, it is true that they do not have as great a self-renewal capacity as embryonic stem cells. Whether or not the degree of self-renewal of an embryonic stem cell is critical is at present not known, and it is likely, for example, that sufficient blood vessel stem cells might be obtained from the bone marrow of a single donor in order to create sufficient blood vessels to enable improvement in heart function.

However, let me just emphasize that as an active investigator and clinician in the field of stem cell biology, I fully support unimpeded funding for ongoing research efforts into both adult and embryonic stem cells. It is too early at present to say whether one or the other type of stem cell approach will prove to be superior for a given disease. But it is probably fair to say that one cell type will not be the answer for all tissue regenerative needs.

Although I am confident that adult stem cells will be the preferred or most adequate way to treat cardiovascular disease, it is too early to make similar conclusions about other disease states such as neurological disorders or diabetes. In these areas, investigators using both types of stem cells are making rapid progress, and future studies will require side-by-side comparisons of each approach.

Major questions concerning the use of embryonic stem cells remain regarding their efficacy for treating various disease states and response to differentiation protocols. In addition, issues about their immunogenicity need to be addressed. So, we come to the potential use of therapeutic cloning of recipient somatic cells using donor eggs.

The concept that these would not be rejected by the recipient's immune system is a solid theoretical argument, data in animal models supporting this concept is scarce. In fact, in last week's issue of *Cell*, a report by Dr. Jaenisch and colleagues outline an extremely unexpected finding, namely rejection of cloned mouse embryonic stem cells which were genetically identical to the recipient by a specific arm of the recipient's own immune response which recognized the cells as foreign. The author suggests that the cloned stem cells were seen as foreign due to their early developmental stage, but it is just as possible that some aspect of the cloning process contributed to their acquiring a foreign nature. As Dr. Jaenisch and his colleagues conclude: "Our results raise the provocative possibility that even genetically matched cells derived by therapeutic cloning may still face barriers to effective transplantation for some disorders."

This emphasizes the early nature of this line of research and highlights the numerous unexpected hurdles that will likely be faced in re-educating the immune system when cloned embryonic stem cells are introduced into a recipient. Moreover, the very process of cloning itself is poorly understood, with investigators having little insight into the causes of its extreme inefficiency, association with abnormal aging, and risk of genetic abnormalities.

Consequently, I believe that consideration of therapeutic cloning of human embryonic stem cells for clinical use is premature. I am concerned that permitting unconditional approval of human embryonic stem cell cloning will result in premature forays into clinical trials by adventurous commercial entities. As outlined above, we need to firstly define which particular diseases are best treated by adult stem cells and which by embryonic stem cells. For those diseases where adult stem cells will not be an option, much work is then needed to understand how to manipulate and differentiate human embryonic stem cells in order to optimize efficacy and minimize risks such as cancer. In parallel, much work should be done in animal models to define methodologies and assess outcomes of using cloned embryonic stem cells. Strict regulation of human embryonic stem cell cloning would not halt progress in these key areas. It will merely ensure the same stringent criteria and safety checks that are applied to other novel therapeutic approaches for human disease.

Rather than delay important research, I believe a moratorium on the clinical use of cloned human cells will prevent hasty and premature experimentation in human subjects without adequate scientific diligence and rigor. For those disease states where embryonic stem cells might be shown to have an advantage over adult cells, their use will be unimpeded in the shorter term by such strict regulatory oversight since they could be used together with low doses of the same immunosuppressive agents currently used to give the average kidney transplant recipient over 10 years of disease-free survival. Therefore, a moratorium on the clinical use of cloned human cells is prudent, encourages much-needed additional work with both human stem cell and cloning technologies, enables close scrutiny of advances in these fields, and allows for review on an intermittent basis to assess the state of scientific progress.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF DR. SILVIU ITESCU

I am Silviu Itescu, Director of Transplantation Immunology at the New York-Presbyterian Hospital of Columbia University in New York. I run a clinical service that provides specialist input into the use and management of immunosuppressive drugs for patients with various solid organ transplants, most notably the heart. Congestive heart failure remains a major public health problem, with recent estimates indicating that end-stage heart failure with two-year mortality rates of 70–80 percent affects over 60,000 patients in the United States each year. In Western societies heart failure is primarily the consequence of previous myocardial infarction or heart attack. Current therapy of heart failure is limited to the treatment of already established disease and is predominantly pharmacological in nature. For patients with end-stage heart failure treatment options are extremely limited, with less than 3,000 being offered cardiac transplants annually due to the severely limited supply of donor organs. Clearly, development of approaches that prevent heart failure after myocardial infarction would be preferable to those that simply ameliorate or treat already established disease.

My research group has recently identified a specific population of stem cells in human adult bone marrow which can be purified and delivered to the heart after a myocardial infarction, enabling the development of many new tiny blood vessels. In a well-characterized animal model this results in protection of heart muscle cells against death through starvation and results in long-term improvement in heart function. We have recently received NIH approval to support funding of further research using these adult stem cells, and are in the process of obtaining our institutional IRB approval to begin safety studies of this therapy in patients with cardiovascular disease.

The notion that adult tissues contain stem cells or progenitors other than those needed to reconstitute bone marrow elements is relatively new, particularly with respect to regeneration of tissues that are not normally renewed, such as cardiac, neuronal or striated muscle. In recent years, several investigators have shown that neural stem cells, as well as hematopoietic and mesenchymal stem cells, can be identified and obtained from adult sources and may give rise to different tissues such as liver, brain, blood, or skeletal muscle, suggesting the presence of one or more types of truly pluripotent stem cells in adults.

While the full developmental options of a given adult stem cell are not yet known, it has recently become evident that environmentally dictated changes of fate may involve progenitor cells at different steps of a given differentiation pathway (trans-differentiation). The adult bone marrow appears to be a particularly rich source of progenitor cells capable of trans-differentiation to cells of various lineages. A striking example of this was the demonstration that transplantation of bone marrow hematopoietic stem cells into genetically defective mice with liver disease resulted in regeneration of liver nodules. In addition to the trans-differentiation potential of hematopoietic stem cells, adult bone marrow cells have been reported to differentiate into neurons when transplanted into normal and ischemic brain. More recently, adult bone marrow-derived cells injected into the spinal cord of rats with spinal cord transection trans-differentiated to become myelin-producing cells. These investigators have suggested that bone marrow cells could, in principle, be harvested from a patient and be used for potential cell therapy approaches in neurological disease.

What all of these recent studies have in common is to emphasize the potential for the use of adult tissue as an alternative source of stem cells to embryonic tissue. If in fact adult tissues contain multipotent stem cells capable of sufficient self-renewal and differentiating capability for use in clinical tissue regeneration, this would provide a far more elegant and preferred approach since autologous cells will not induce any immunologic rejection and no immunosuppression will be needed. In contrast, embryonic stem cells will always be seen as foreign by the recipient, and some degree of immunosuppression is likely to be required. While adult bone marrow stem cells appear to have the ability to replicate to greater levels than other adult, differentiated cell types, it is true that they do not have as great a self-renewal capacity as embryonic stem cells. However, at present it is not known what degree of self-renewal capacity is needed in order for a stem cell to be capable of providing sufficient progeny for clinical use. For example, it is likely that sufficient blood vessel stem cells can be obtained from the bone marrow of a single donor in order to create sufficient new blood vessels to enable improvement in heart function.

As an active investigator and clinician in the field of stem cell biology I fully support unimpeded funding for ongoing research efforts into both adult and embryonic stem cells. It is too early at present to say whether one or the other type of stem cell approach will prove to be superior for a given disease, but it is probably fair to say that one cell type will not be the answer for all tissue regenerative needs. Although I am confident that adult stem cells will be the preferred and most adequate way to treat cardiovascular disease, it is too early to make similar conclusions about other disease states such as neurological disorders or diabetes. In these areas investigators using both types of stem cells are making rapid progress, and future studies will require side-by-side comparisons of each approach.

Major questions concerning the use of embryonic stem cells remain regarding their efficacy for treating various disease states, risk of cancerous transformation, and response to differentiation protocols. In addition, issues about their immunogenicity need to be addressed. In order to overcome the last problem, which is also the major perceived advantage of adult stem cells, a number of investigators have suggested the use of "therapeutic cloning" of recipient somatic cells using donor eggs. The resulting embryonic stem cells would have all of the genetic material of the recipient, and thus not be rejected by the recipient's immune system.

While this is a scientifically solid theoretical argument, data in animal models supporting this concept are scarce. In fact, in last week's issue of *Cell* a report by Jaenisch and colleagues outlined an extremely unexpected finding, namely rejection

of cloned embryonic stem cells genetically identical to the recipient by a specific arm of the recipient's immune response which recognized the cells as foreign due to their early developmental stage. This emphasizes the early nature of this line of research, and highlights the numerous unexpected hurdles that will likely be faced in re-educating the immune system. Moreover, the very process of cloning itself is poorly understood, with investigators having little insight into the causes of its extreme inefficiency, association with abnormal cellular senescence, and risk of genetic abnormalities. Whether cloned embryonic stem cells will demonstrate similar defects, whether they will have greater susceptibility to cancerous transformation, and more importantly whether the regenerative potential of such cells is affected by the cloning process itself, is at present unknown. These questions will need to be adequately addressed in numerous animal models before one would consider performing such studies in humans.

I believe that consideration of therapeutic cloning of human embryonic stem cells is premature. As outlined above, we need to firstly define which particular diseases are best treated by adult stem cells and which by embryonic stem cells. For those diseases where adult stem cells will not be an option, much work is then needed to understand how to manipulate and/or differentiate human embryonic stem cells in order to optimize efficacy and minimize risk of cancer. In parallel, much work should be done in animal models to define methodologies and assess outcomes of using cloned embryonic stem cells. A moratorium on human embryo cloning would not halt progress in these key areas, it will merely ensure the same stringent criteria and safety checks that are applied to other novel therapeutic approaches for human diseases. Rather than delay important research, I believe a moratorium on human cloning will prevent hasty and premature experimentation in human subjects without adequate scientific diligence and rigor. For those disease states where embryonic stem cells might be shown to have an advantage over adult stem cells, their use will be unimpeded by such a moratorium since they could be used together with low doses of the same immunosuppressive agents currently used to give the average kidney transplant recipient over ten years of disease-free survival. A moratorium on human embryo cloning is prudent, encourages much-needed additional work with both human embryonic and cloning technologies, enables close scrutiny of advances in these fields, and should be reviewed on an intermittent basis to assess the state of scientific progress.

Senator SPECTER. Thank you very much, Dr. Itescu.

We now turn to Mr. Kevin Kline who won an academy award for his performance in "A Fish Called Wanda." He is known for his roles in "Sophie's Choice," "Dave," and "Soapdish." He is a graduate of the Julliard School of Drama, received the Shakespeare Award for classical theater from the Shakespeare Theater here in Washington, as well as two Obie Awards. Thank you for joining us, Mr. Kline, and we look forward to your testimony.

STATEMENT OF KEVIN KLINE, ACTOR

Mr. KLINE. Thank you, Mr. Chairman. Thank you for the opportunity of appearing before you.

As you said, my name is Kevin Kline. I am an actor. I am also a member of the board of the directors of the New York Chapter of the Juvenile Diabetes Research Foundation, serving as vice president of Public Outreach and Education. Today I appear simply as a private citizen who, like many others, has witnessed firsthand the devastating ravages of diseases such as Alzheimer's, diabetes, and Parkinson's, and who, like many others, have seen a bright light at the end of the tunnel, that light being the hope given by the potential promise of stem cell research.

Medical research is finally moving beyond the ability to describe dysfunctional, disease-causing cell behavior to being able to change cell activity in order to eliminate disease and deterioration of organs and tissue. We are all privileged to be alive at the beginning of the most promising era in life science and I am deeply troubled

that critical scientific research may meet extinction at the hands of legislation pending before this Congress.

Throughout our history medical science has brought miraculous cures, often in the face of strong opposition by those who fear that scientists are going too far and are tampering with nature. In this country, our Government has always had the wisdom to regulate not prohibit cutting edge scientific research.

The efforts of the global scientific community have made it possible to create cells with the DNA of patients to be treated using unfertilized eggs and a scientific technique called nuclear transplantation. Nuclear transplant research may be the key to helping scientists understand why cells malfunction and how to deprogram and reprogram these cells to function normally.

The Senate is considering whether to make the conduct of promising nuclear transplant research a Federal criminal offense. Opponents of nuclear transplant research chide patients and parents not to be hoodwinked by the biotechnology industry, which they warn us is promoting scientific research for financial gain, which parenthetically I do not understand why we give credence and billions of dollars to our Nation's scientists who develop smart bombs and fantastic defense systems, and yet we are suspicious of our medical scientists who are developing medical technologies, accusing them of doing so for financial gain.

Opponents further admonish the scientific community not to raise the hopes of sick children and adults and their families now when a cure may be far away. With all due respect, these families are not listening to salesmen. They are listening to scientists, and they are not naive. These families know as much about their children's diseases as many doctors. They have made it their business to do so. Many families have seen hereditary conditions ravage their loved ones for generations. These families and their loved ones deserve access to the best medical treatment that we hope will result from future research.

I am not a scientist. I have not even played a scientist on TV.

But I know that the majority of the brightest minds in science throughout the world believe that this research is not only promising, but that stem cell research and nuclear transplantation could represent a new frontier in medicine and potentially a giant step in the history of man's quest to ease human suffering.

I know there are those who disagree. There always have been and there always will be. And I thank God that we live in a country where freedom of thought and the right to private judgment in matters of conscience is allowed. Scientific inquiry and religious dogma have, by their nature, always been uneasy bedfellows.

Now, if you have made a decision to say no to the possibilities of this research or, like some, contend that even if we had a cure using nuclear transplantation, you would not use it, then it is your inalienable right, and I doubt that I will be able to change your mind. But please, I implore you, do not deny the rest of us our access to the best medical technology available or the fruits of the best medical researchers. And if the next miracle comes from Canada or England, Ireland, Scotland, or Sweden, I want to be allowed to take my child there and not face imprisonment when we return, as the Brownback legislation mandates.

I believe there is no moral high ground in letting people suffer and die in staggering numbers because of a fear of something clearly that no one wants: human reproductive cloning. Congress can and should ban reproductive cloning.

I think, on the contrary, though, we have a great moral obligation to pursue this new scientific research. In America, we have the best and brightest medical minds in the world. One need only spend a few minutes in the pediatric ward of a hospital in order to see perhaps a 5-year-old child with no hair on his head from chemotherapy or the look on the face of a child just diagnosed with juvenile diabetes, condemned to an abbreviated lifetime of insulin injections and the continual fear of complications, such as kidney failure, blindness, or amputation. In the face of this, it is impossible to walk away without thinking it is shameful not to pursue any and all promising research that could lead to a cure or prevention.

If we criminalize those who have dedicated their lives to our health, if we allow millions of people to die every year because we fear science, then we have not taken the moral high ground. Rather than criminalize it, I believe the Government should fund this research and regulate it.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF KEVIN KLINE

My name is Kevin Kline. I am an actor and the Vice-President of Public Outreach and Education for the New York Chapter of the Juvenile Diabetes Research Foundation. Today I appear as a private citizen, who, like so many others, has witnessed first hand the devastating ravages of diseases such as Alzheimer's, diabetes and Parkinson's, and, too, like many others have seen a bright light at the end of the tunnel—that light being the hope given by the potential promise of stem cell research.

Medical research is finally moving beyond the ability to describe dysfunctional, disease-causing cell behavior to being able to change cell activity in order to eliminate disease and the deterioration of organs and tissue. We are all privileged to be alive at the beginning of the most promising era in life science and I am concerned that critical scientific research may meet extinction with legislation pending before this Congress.

Throughout history, medical science has brought us miraculous cures, often in the face of strong opposition by those who fear that scientists are going too far and are tampering with nature. In this country, our government always has had the wisdom to regulate, not prohibit, cutting edge scientific research.

The efforts of the global scientific community have made it possible to create cells with the DNA of patients to be treated, using unfertilized eggs and a scientific technique called "nuclear transplantation." Nuclear transplant research may be the key to helping scientists understand why cells malfunction and how to deprogram and reprogram these cells to function normally.

The Senate is considering whether to make the conduct of promising nuclear transplant research a federal criminal offense. Opponents of nuclear transplant research chide patients and parents not to be hoodwinked by the biotechnology industry, which they warn is promoting scientific research for financial gain. Patients and their families are not naive; they are listening to scientists, not salesmen. Opponents further admonish the scientific community not to raise the hopes of sick children and adults and their families now, when a cure may be far away. Many families have seen hereditary conditions ravage their loved ones for generations. These families don't need the government to protect them from hope, and they deserve access to the best medical treatment that we all hope will result from future research.

I am not a scientist—I have not even played the part of a scientist—but I know that overwhelmingly the brightest minds in science throughout the world believe that this research is not only promising, but that stem cell research and nuclear

transplantation represent a new frontier in medicine and potentially a giant step in the history of man's continued triumph in the quest to ease human suffering.

I believe there is no moral high ground in letting people suffer and die in staggering numbers because of a fear of something that no one wants: human reproductive cloning. The government can and should ban human reproductive cloning.

I think, in fact, we have a great moral obligation to pursue this new scientific research. In America we have the best and brightest medical minds in the world. If we do not allow them to save lives and diminish suffering—if we criminalize those who have dedicated their lives to our health—if we allow millions of people to die every year because we fear science—then we have not taken the moral high ground. For our government to criminalize nuclear transplant research would be a crime.

Senator SPECTER. Thank you very much, Mr. Kline.

Dr. Fischbach, on the issue of the effectiveness of nuclear cell transplant and the studies conducted by Dr. Rudolph Jaenisch, what is your evaluation of the tests showing that therapeutic cloning works?

Dr. FISCHBACH. I think that paper, which just appeared a few days ago, was extraordinary. I had a chance to look at it quickly. The big news from that paper is that it does work. The fact that there may still be residual problems with immune rejection was considered a minor issue in that paper, one to be paid attention to and explored further. Unexpected. But the major point in that paper is that nuclear transfer, coupled with genetic engineering of the stem cells so derived, could reverse a devastating disorder of immune deficiency in these model organisms. It holds great promise, enormous promise for application to human disorders of immune deficiency.

The residual problem of the rejection of the cells eventually may have several explanations. The cells were grown in tissue culture for a while. There may be some other modification. And that points out the need for more extensive research on the stem cells. But the paper, as it stands, is a great tribute to the promise of somatic cell nuclear transfer.

Senator SPECTER. Dr. Itescu, are you familiar with that paper and able to give us your judgment on it?

Dr. ITESCU. Yes. I would agree that the scientists were clearly able to reverse the genetic defect through gene repair in the embryonic stem cells and demonstrated the ability of the embryonic stem cells, even after cloning, to be functionally capable of regenerating the defect.

However, the problem about the rejection is a serious problem. It is an example that there are many hurdles that need to be overcome in using cloned cells in the recipient.

Senator SPECTER. What hurdles are those, Dr. Itescu?

Dr. ITESCU. The underlying concept that a cloned cell will not be rejected by the recipient I think has to at least be challenged by these results, and I think there are many possible explanations, including the fact that—

Senator SPECTER. So, those hurdles are challenged by the results of the study that Dr. Fischbach and you were testifying about?

Dr. ITESCU. I think that there are hurdles that have been raised through the results of this paper, and I think it emphasizes why research needs to be done, needs to go forward in many animal models because there will be surprising hurdles that will come up. I think it emphasizes how much more support this type of research requires prior to jumping into the clinical arena.

Senator SPECTER. But you do favor additional research.

Dr. ITESCU. Absolutely.

Senator SPECTER. And you would oppose criminal penalties for the researchers who move into the area of nuclear transplantation, or so-called therapeutic cloning?

Dr. ITESCU. I would oppose criminalization of the researchers.

Senator SPECTER. Do you think it might drive people back to Australia?

Dr. ITESCU. I think so.

Senator SPECTER. Do they have any criminal laws on this subject in Australia?

Dr. ITESCU. I think the debate is still ongoing in Australia regarding this area.

Senator SPECTER. You say there is debate?

Dr. ITESCU. There is currently debate on the same issues.

Senator SPECTER. The same as here. But they have not criminalized it.

Dr. ITESCU. No.

Senator SPECTER. Dr. Fischbach, what do you think would be the consequence of legislation being passed which criminalized this kind of research? Would we have an exodus of any significant proportion?

Dr. FISCHBACH. I think there will be an exodus of scientists, but it will extend even beyond that. I think it will cast a pall over scientific research over a broad area. It will be the first time ever that inquiry has been subject to criminal penalties of this sort. So, I believe that it will stop stem cell research. It will not stop it cold, but it will severely limit it. It will be discouraging for senior and junior scientists to continue in this field, and I think those absolutely committed will emigrate where they can do the work. But this is leaving family, friends, and institutions, and it will cause great havoc I believe in the institutions.

Senator SPECTER. Dr. Fischbach, you represent a coalition of some 60 universities. It is really important that there be a massive effort by those universities to contact Senators. The most effective way to have the influence is to contact Senators in their States. We can provide you a list.

Tennessee is high on the agenda with Dr. Bill Frist who made some comments in a hearing held last year before the Health, Education, and Pension Committee where I testified. Dr. Frist is our sole doctor Senator, so he has somewhat more weight on the subject. And I only use Senator Frist illustratively, but there needs to be that kind of activity.

We are writing to the editorial boards of the newspapers in America and the talk shows to develop a public awareness. The bill passed, as you heard, by 260-some votes to 160 in the House, but they only had an hour and 10 minutes of debate. I believe that with the unlimited debate we have in the Senate, we can focus a bit more attention. But the proponents of keeping the hands of scientists untied are going to have to really work hard to join those of us on this issue who are in favor of scientific freedom.

Mr. Kline, as an actor, you enjoy a profession which is widely recognized. I do not see one camera focused on Dr. Fischbach in this room at the moment.

Not one camera focused on Dr. Itescu at the moment.

Dr. FISCHBACH. I am used to it.

Senator SPECTER. Well, you are going to have to become an orator of sorts, perhaps not an actor, Dr. Fischbach, but you are going to have to make your voice heard in many, many places through your coalition.

But, Mr. Kline, what would your suggestion be? This is not your direct field of public persuasion, yet you influence a lot of people with what you say. Would you have any suggestions as to how we might carry on this campaign, and use the public interest in all of the personalities you portray, to make them aware of the importance of not tying scientists' hands and allowing medical research to go forward?

Mr. KLINE. I think clarity is what the American people would relish, to understand, A, what we do know about stem cell research and to understand that there is this enormous gray area that we do not understand. Many of us in the lay community are talking about these things that we really only know the tip of the iceberg about. I think as such, whether we are Senators, Congressmen, actors, lobbyists, it must all be taken into account that perspective and with a grain of salt. We do not know what it is.

My argument is that how can we close that door, how can we not go down that road to find out what lies ahead with this research? How can we, in fact, criminalize it? It is medieval to me. I think if we just admit what we do know and admit what we do not know—and what constitutes life is, as you said earlier, a subject of great personal, private introspection, and it is something between the individual and his god. I do not know that we can legislate as either a governmental agency or as a scientific agency or as a religious agency. Every religion is going to have their own definition of what constitutes human life. It is a very murky subject.

I think it comes down to a matter of compassion for life that is being lived, life in progress that is afflicted with a mortal disease with a heretofore unknown cure. It is weighing that against the potential of what may or may not be a form of human life.

Senator SPECTER. Well, we are facing a very difficult situation. We are facing a bill which has been passed in the House and that the President will sign. What we need to do is focus public attention on it, and we need a national debate on the subject. We need people to act in a representative democracy—that is what we have, a republic, a representative democracy—to contact their legislators and express their opinions. If the Brownback bill wins, so be it, it wins, in a democracy. But there ought to be a maximum effort to acquaint the public with the situation so that we have that debate and we have a rational decision, and if we do that, I believe that nuclear transplants will prevail and scientists will not have their hands tied.

Senator Mack's illustration on the fire could be duplicated—in the 19th century when the House of Commons passed a resolution saying that electricity and Edison's efforts could never replace gas. And when Galileo went to jail for supporting Copernicus that the earth was not flat. The church took a position against dissecting cadavers in the 13th century which set back medical research 300 years. The Scottish church opined against the use of anesthesia in

the 18th century, saying that it was natural for women to endure pain during childbirth. Those are but a few of the examples of legislators, politicians tying the hands of scientists.

So if, in your world, Mr. Kline, you know any television shows which are writing scripts in the next couple of weeks to carry this message. I have already given Dr. Fischbach his charge of moving ahead. And, Dr. Itescu, we want to keep you here. We do not want you going back to Australia.

So, join us in this effort to have a rational judgment made on this question so as not to have a brain drain, and not to have the hands of scientists tied, and not to undercut the tremendous opportunities we have with stem cells.

For the record, we are going to include a statement by the Union of Orthodox Jewish Congregations, representing nearly 1,000 congregations and the Rabbinical Council of America whose membership consists of more than 1,000 rabbis. I would ask that the joint statement entitled "Cloning Research: Jewish Traditions and Public Policy" be placed in the record, a statement which supports nuclear transplant, so-called therapeutic cloning, but opposes cloning for reproductive purposes.

[The statement follows:]

PREPARED JOINT STATEMENT OF THE UNION OF ORTHODOX JEWISH CONGREGATIONS
OF AMERICA AND THE RABBINICAL COUNCIL OF AMERICA

CLONING RESEARCH, JEWISH TRADITION & PUBLIC POLICY

Society today stands on the threshold of a new era in biomedical research. The wisdom granted to humans by our Creator has led to our greater understanding and knowledge of the building blocks of human life itself. Scientists revealed the existence and role of DNA and cellular science many years ago. Currently, scientists are not only able to describe the nature of cellular life, but manipulate it as well. We are now faced with the possibility of mastering the art of this manipulation to the point of being able to clone in research laboratories the cells that, in other circumstances, lead to fully developed human beings.

A debate has emerged in American society at large and among our elected leaders as to whether public policy should permit, encourage, restrict or ban the further conduct of this biomedical research. The issue is one with complex moral dimensions. On the one hand scientific research indicates that there is great life-saving potential in the results that can come from cloning research.¹ On the other hand, we must be vigilant against any erosion of the value that society accords to human life.

Our Torah tradition places great value upon human life; we are taught in the opening chapters of Genesis that each human was created in God's image. After creating man and woman, God empowered them to enter a partnership with Him in the stewardship of the world. The Torah commands us to treat and cure the ill and to defeat disease wherever possible; to do this is to be the Creator's partner in safeguarding the created. The traditional Jewish perspective thus emphasizes that maximizing the potential to save and heal human lives is an integral part of valuing human life. Moreover, our tradition states that an embryo in vitro does not enjoy the full status of human-hood and its attendant protections. Thus, if cloning technology research advances our ability to heal humans with greater success, it ought to be pursued since it does not require or encourage the destruction of life in the process.

However, cloning research must not be pursued indiscriminately. We must be careful to distinguish between cloning for therapeutic purposes—which ought to be pursued, and cloning for reproductive purposes—which we oppose. Thus, this research must be conducted under strict guidelines and with strict limitations to ensure that the research is indeed serving therapeutic purposes.

¹ This joint statement specifically addresses our view on the subject of cloning technology research. We have previously set forth our views on the related subject of stem cell research in a document which may be found at <http://www.ou.org/public/Publib/cloning.htm>

Consistent with this policy, we advocate that a fully funded and empowered oversight body comprised of scientists and ethicists be created to monitor this research. Relevant Executive-branch agencies and congressional committees should conduct periodic reviews as well. The oversight process should pay special attention to ensuring that the embryos used in this research are not brought to a point which constitutes human-hood.

We believe that the policy stated herein articulates the perspective of the Torah tradition and the community we represent and achieves the correct balance between pursuing new methods for saving human lives and maintaining the fundamental respect and sanctity of human life.

CONCLUSION OF HEARINGS

Senator SPECTER. Thank you all very much for being here, that concludes our hearings.

[Whereupon, at 3:25 p.m., Tuesday, March 12, the hearings were concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

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